

Quantifying states of consciousness by means of intrinsic brain connectivity

**Institute of Neuroscience and Medicine,
Brain & Behaviour (INM-7)
Research Centre**

September 12 2019, Jülich, Germany

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FNRS Research Associate

Physiology of Cognition Research Lab | GIGA Consciousness | GIGA Institute

University of Liège Belgium



ADemertzi



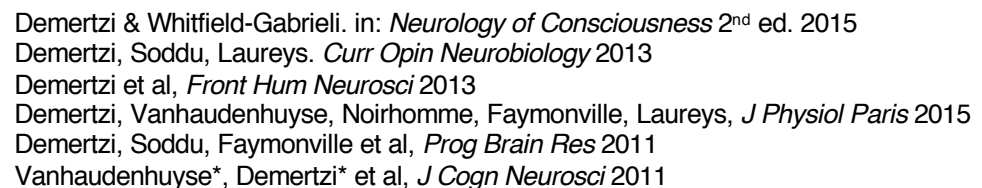
a.demertzi@uliege.be





What is Consciousness?

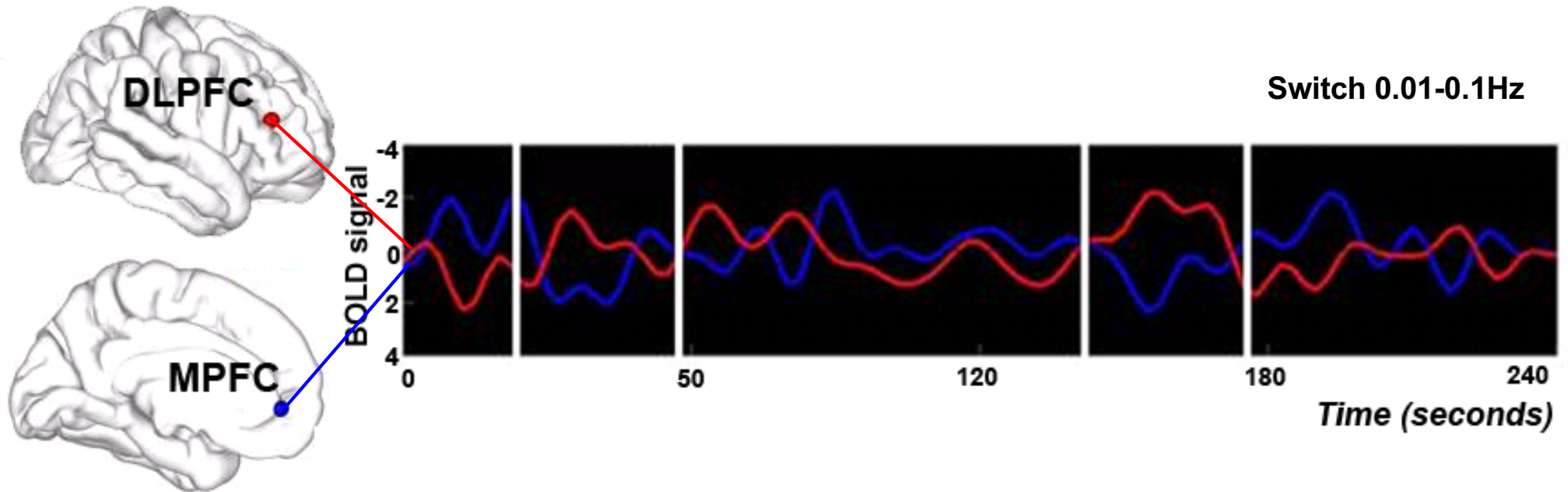






A mode of awareness?

**External awareness
or anticorrelated network**



**Internal awareness
or Default mode network**

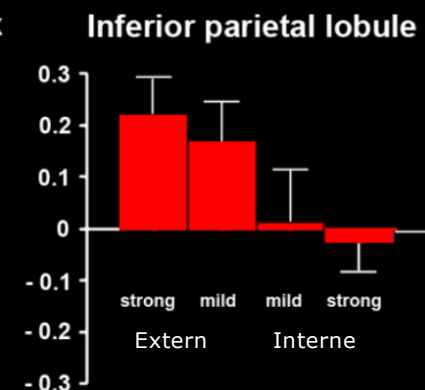
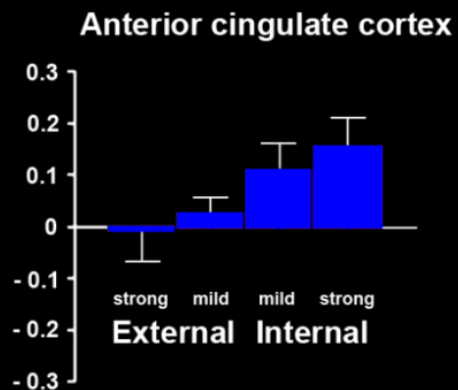
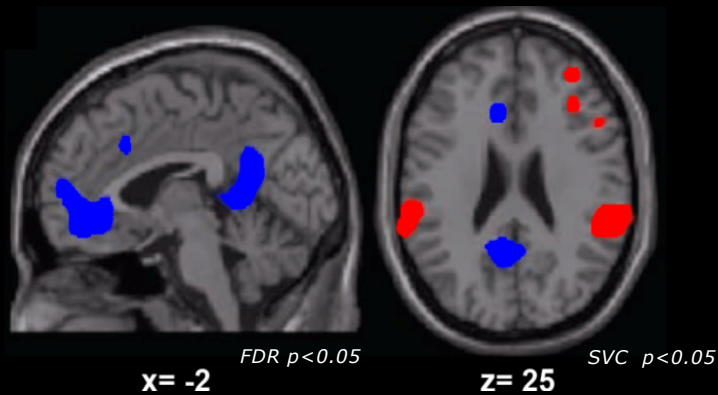
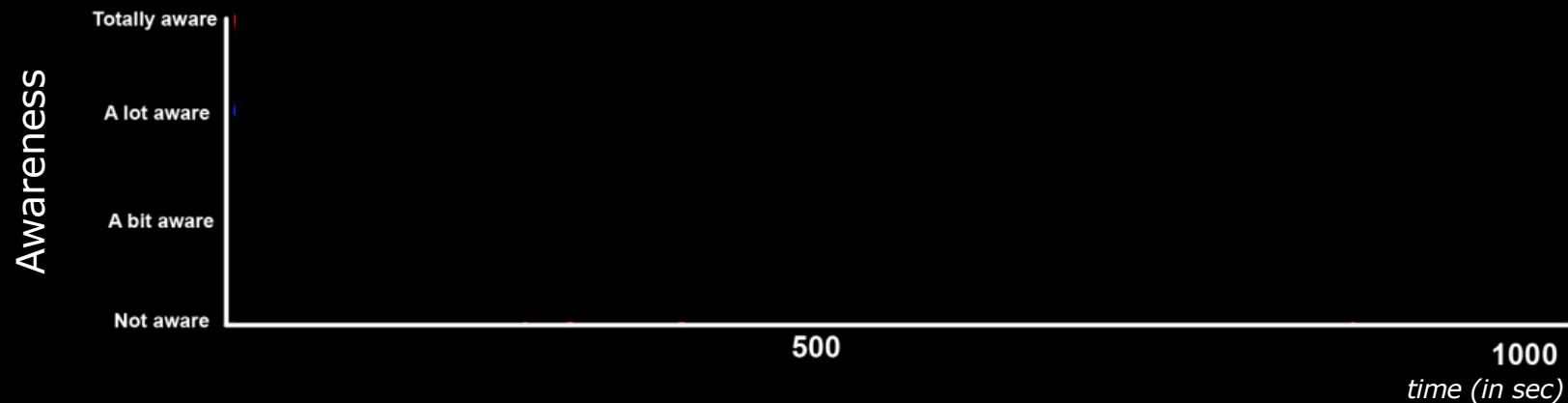
Demertzi, Soddu, Laureys, *Curr Opin Neurobiology* 2013
Demertzi & Whitfield-Gabrieli, in: *Neurology of Consciousness* 2nd ed. 2015
Demertzi et al, *Front Hum Neurosci* 2013
Laureys, *Scientific American* 2007
Fox et al, *PNAS* 2005

Neurobehavioral relevance of the anticorrelations



■ Internal awareness
■ External awareness

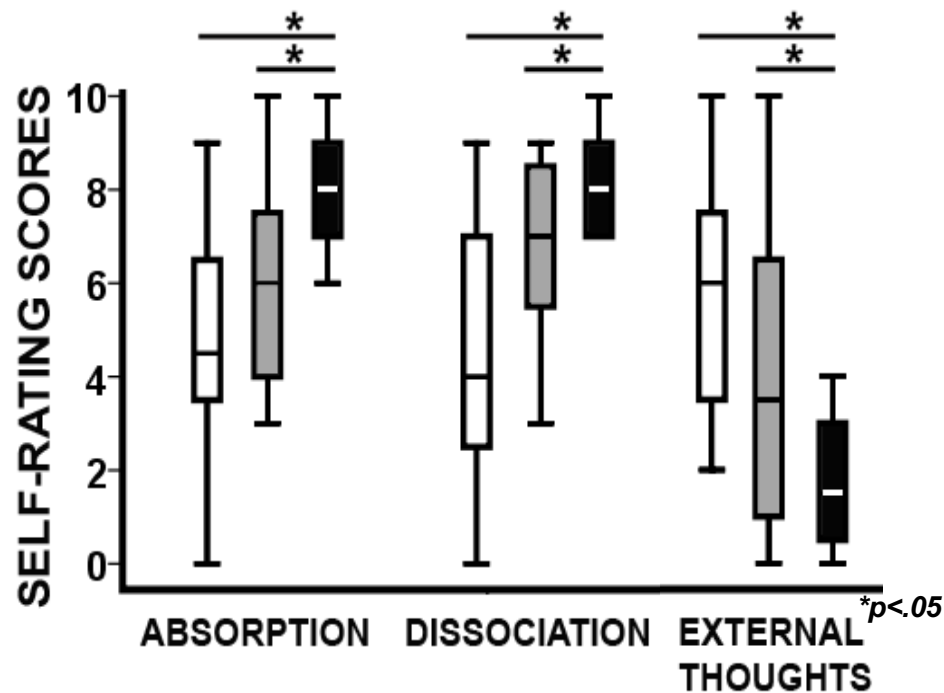
External-internal: $r = -0.44$, $p < .02$
 Mean switch: 0.05Hz (range: 0.01-0.1)



Anticorrelated connectivity is modified in hypnosis-Brain

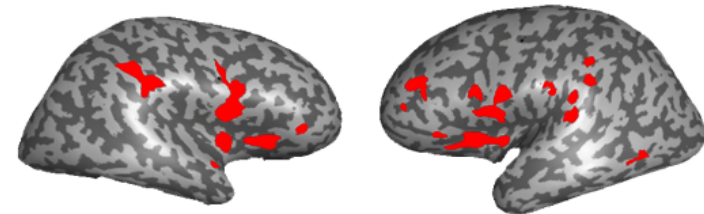


- Normal consciousness
- Autobiographical mental imagery
- Hypnosis

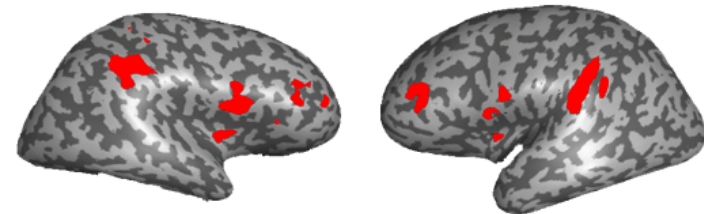


EXTRINSIC SYSTEM

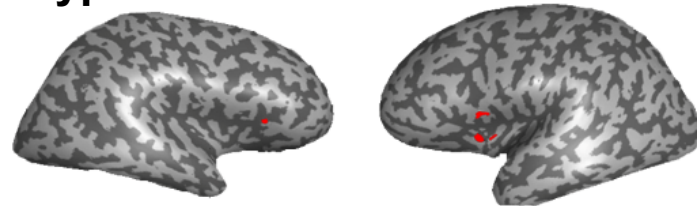
Normal consciousness



Autobiographical mental imagery

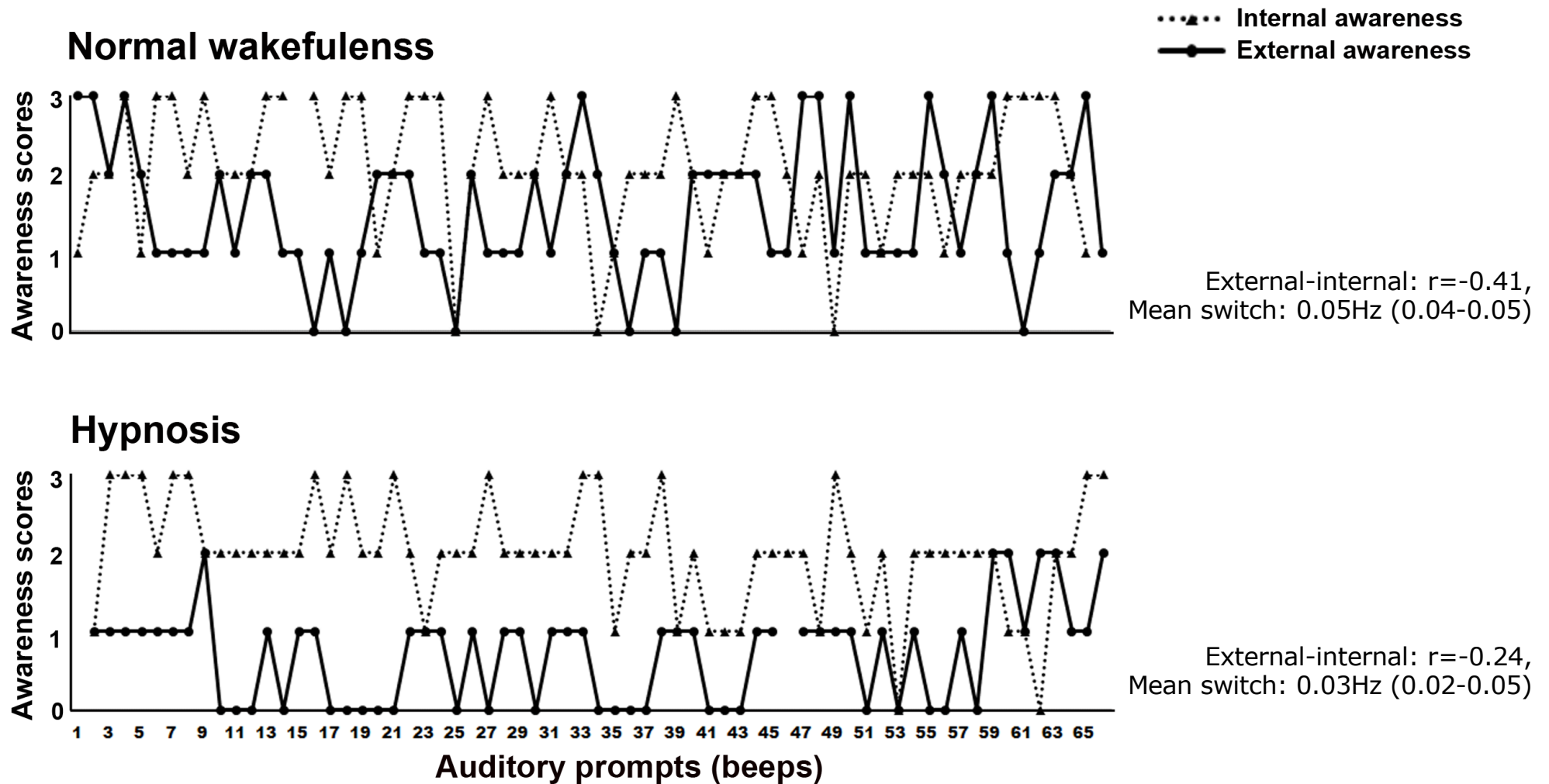


Hypnosis



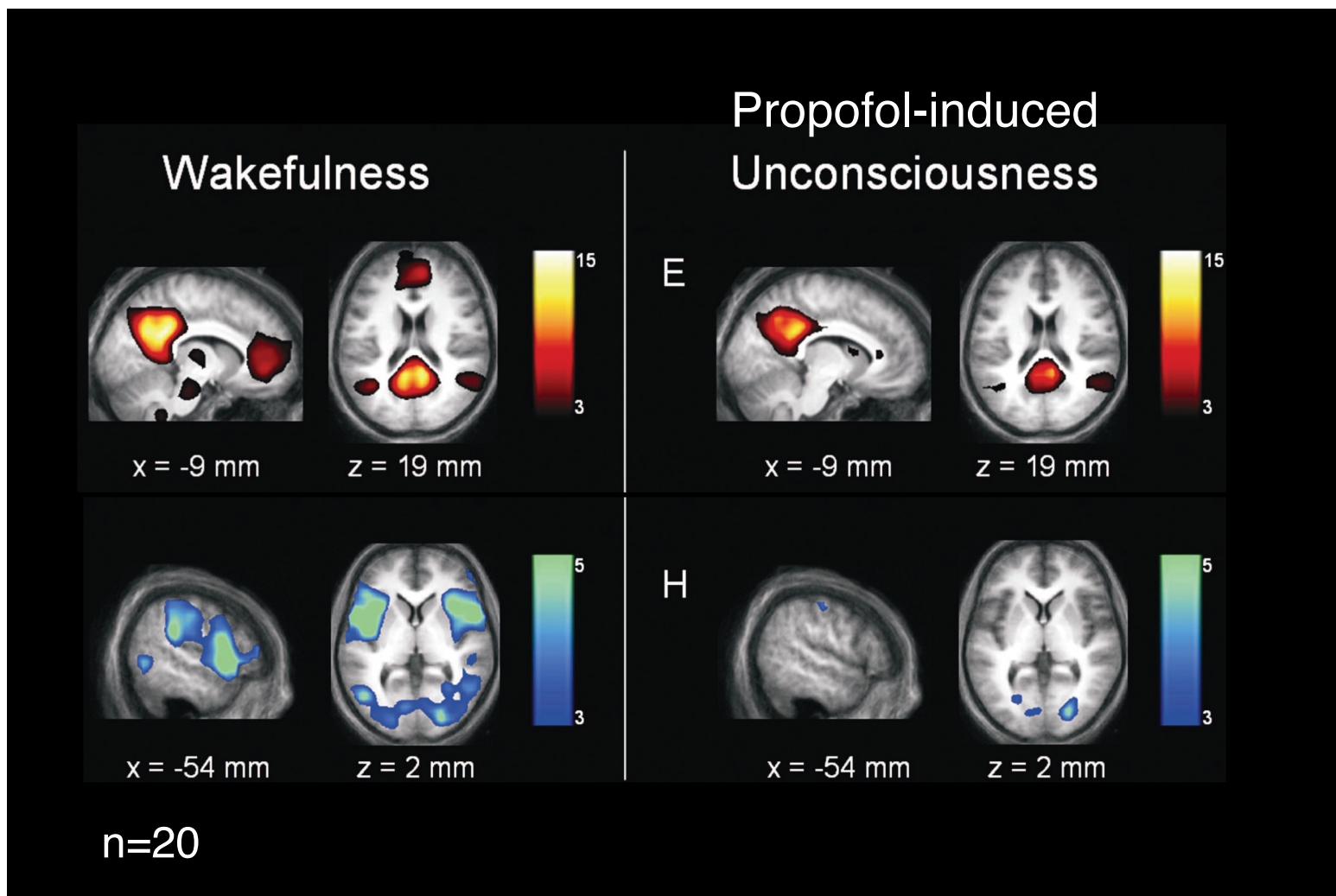
$p < 0.05$ corrected for multiple comparisons

Anticorrelated connectivity is modified in hypnosis-Behavior





Anticorrelations reduce in anesthesia





Effect of environment

SCIENTIFIC REPORTS

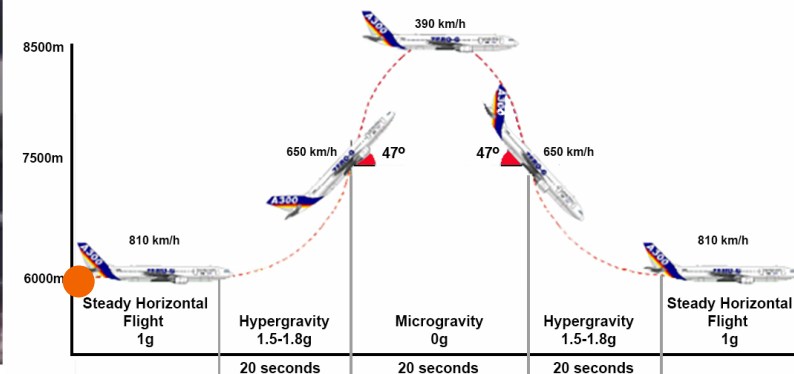
www.nature.com/scientificreports/



Parabolic flight



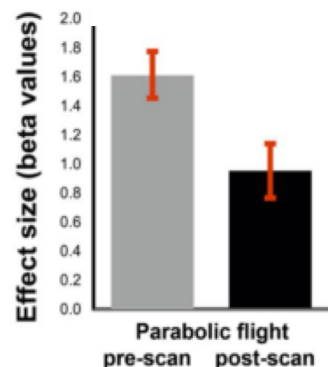
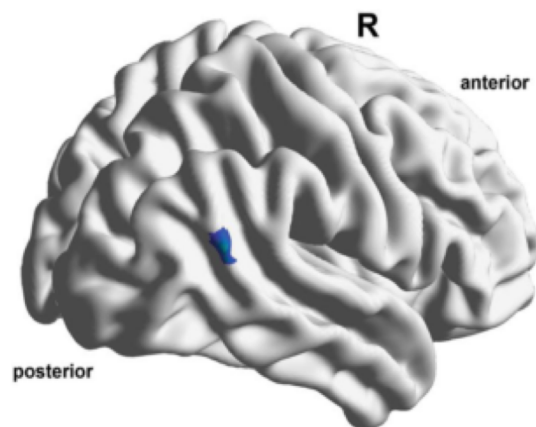
European Space Agency



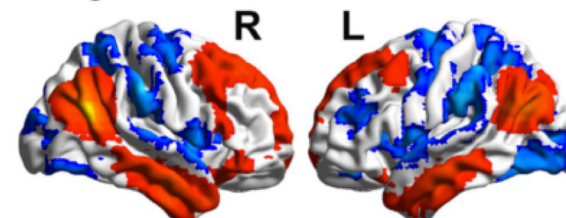
Parabolic flight trajectory

Angelique Van Ombergen¹, Floris L. Wuyts¹, Ben Jeurissen², Jan Sijbers², Floris Vanhevel³, Steven Jillings¹, Paul M. Parizel³, Stefan Sunaert⁴, Paul H. Van de Heyning¹, Vincent Dousset⁵, Steven Laureys⁶ & Athena Demertzi^{6,7}

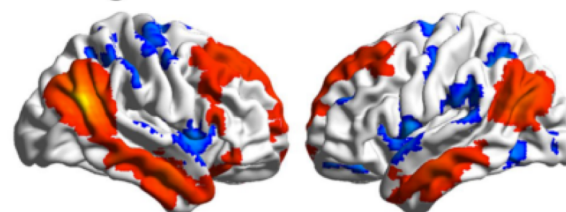
Anticorrelations reduce in extreme environments



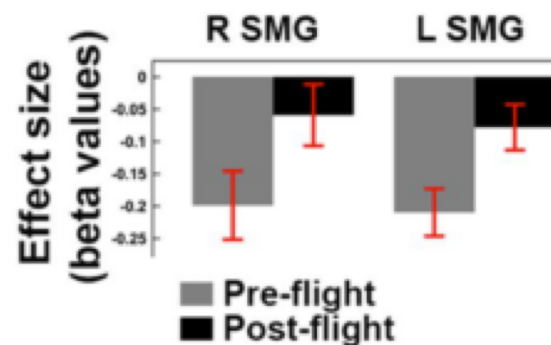
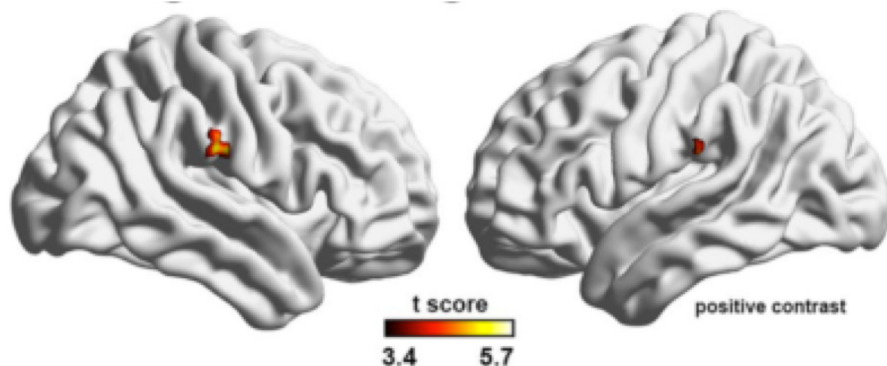
Pre-flight



Post-flight

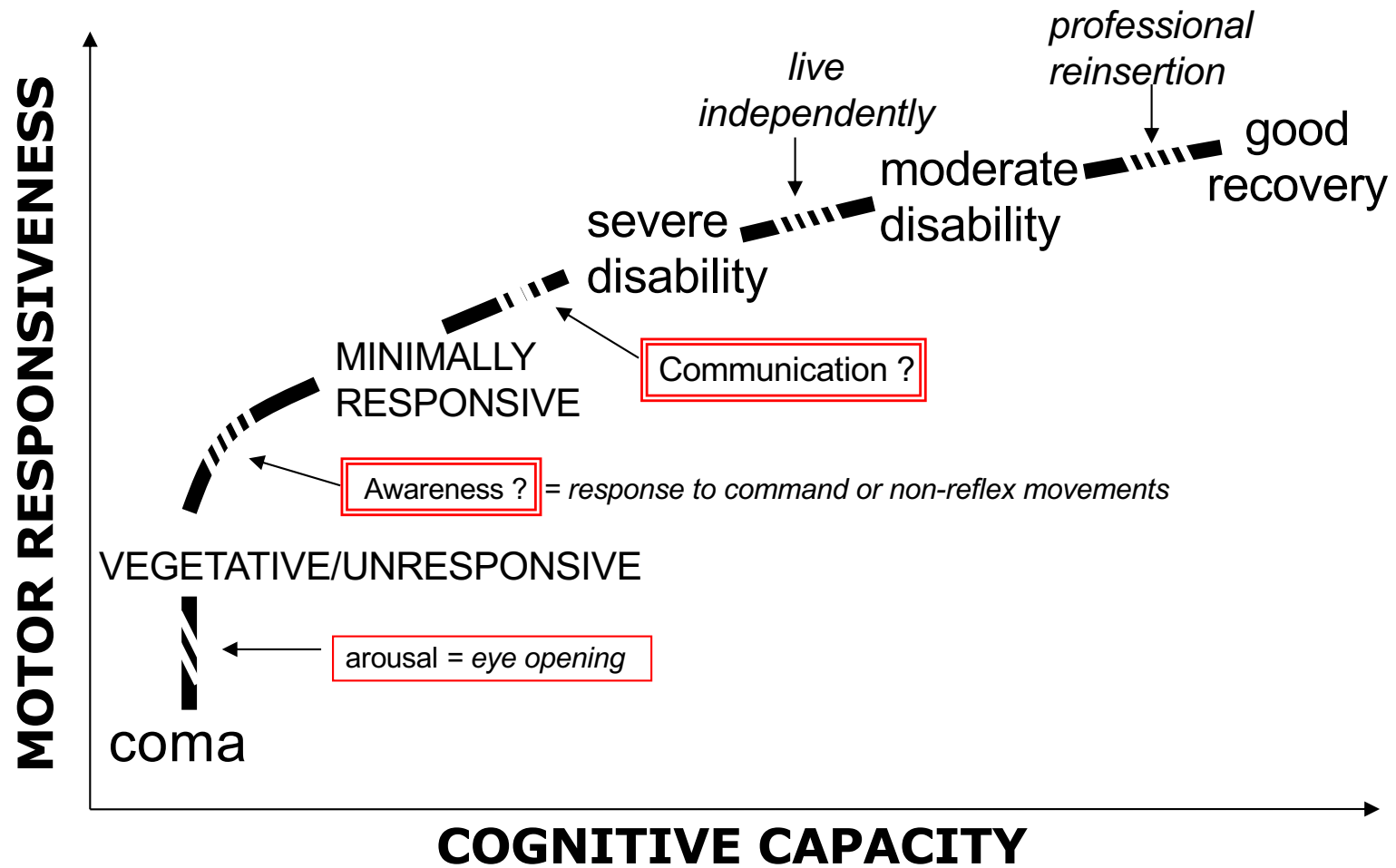


Post – Pre flight

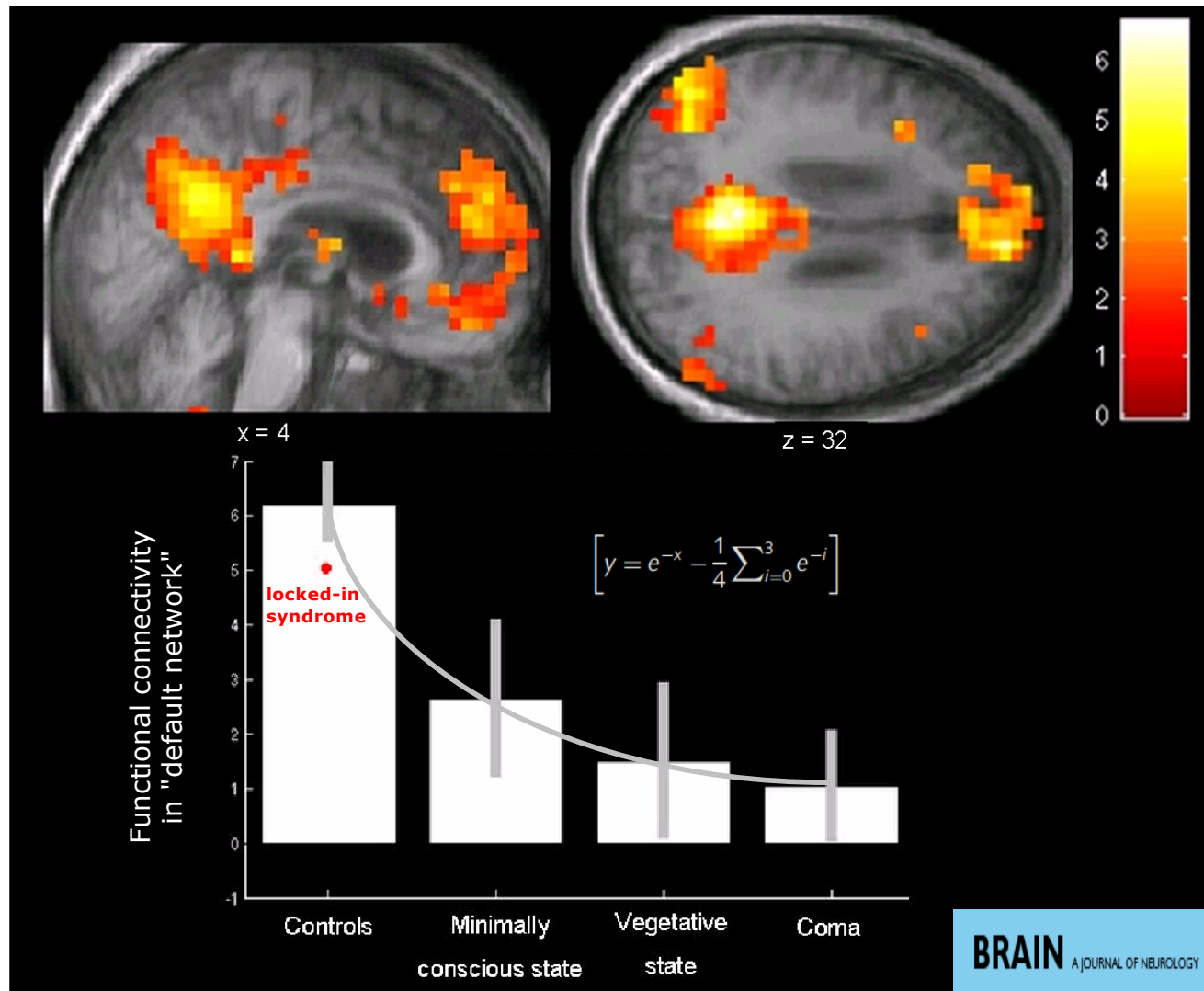




Disorders of Consciousness

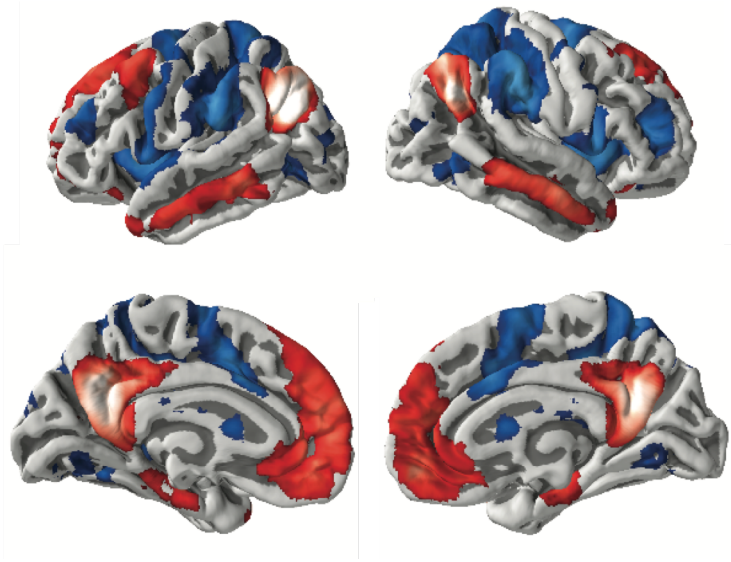


Default mode network in DOC

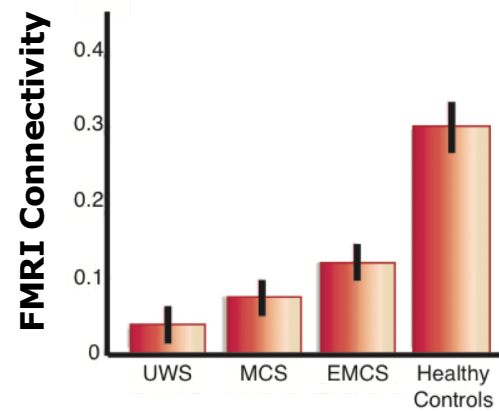




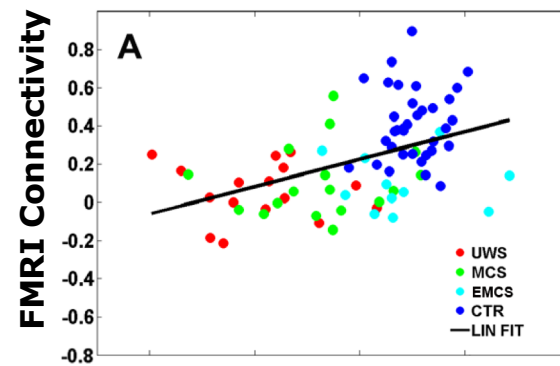
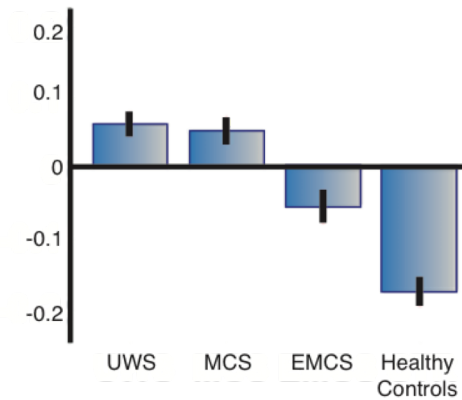
Effect of pathology



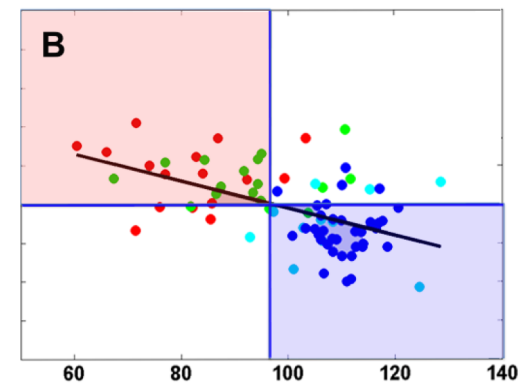
DMN CORRELATIONS



DMN ANTICORRELATIONS

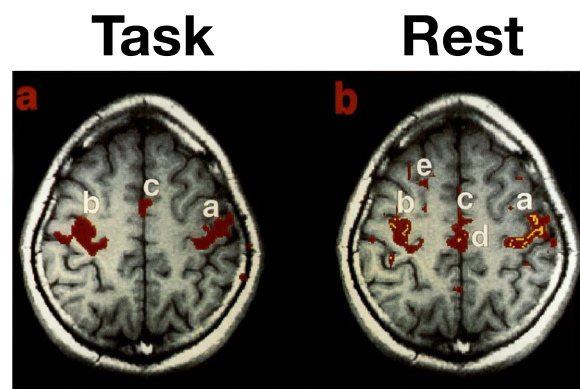


Brain metabolism

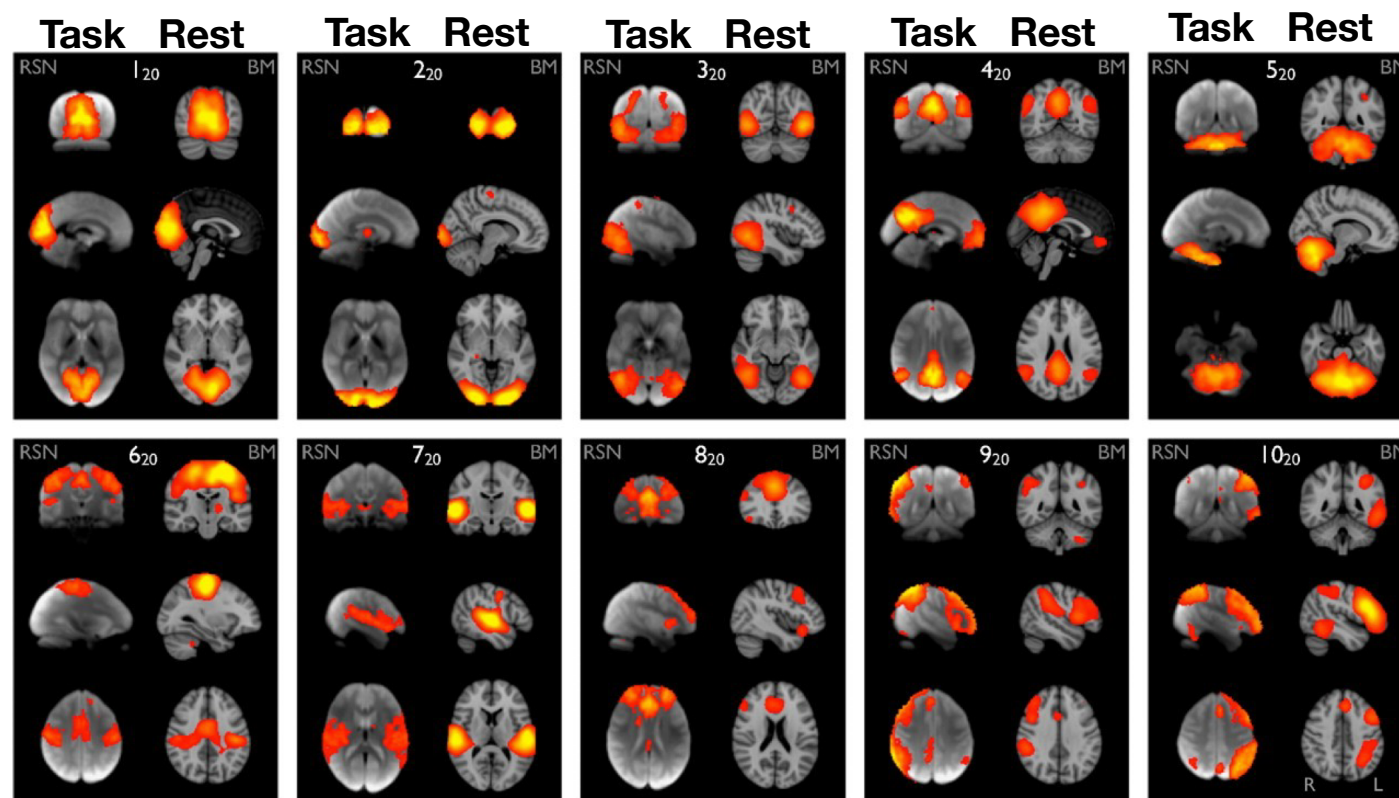




Intrinsic Connectivity Networks

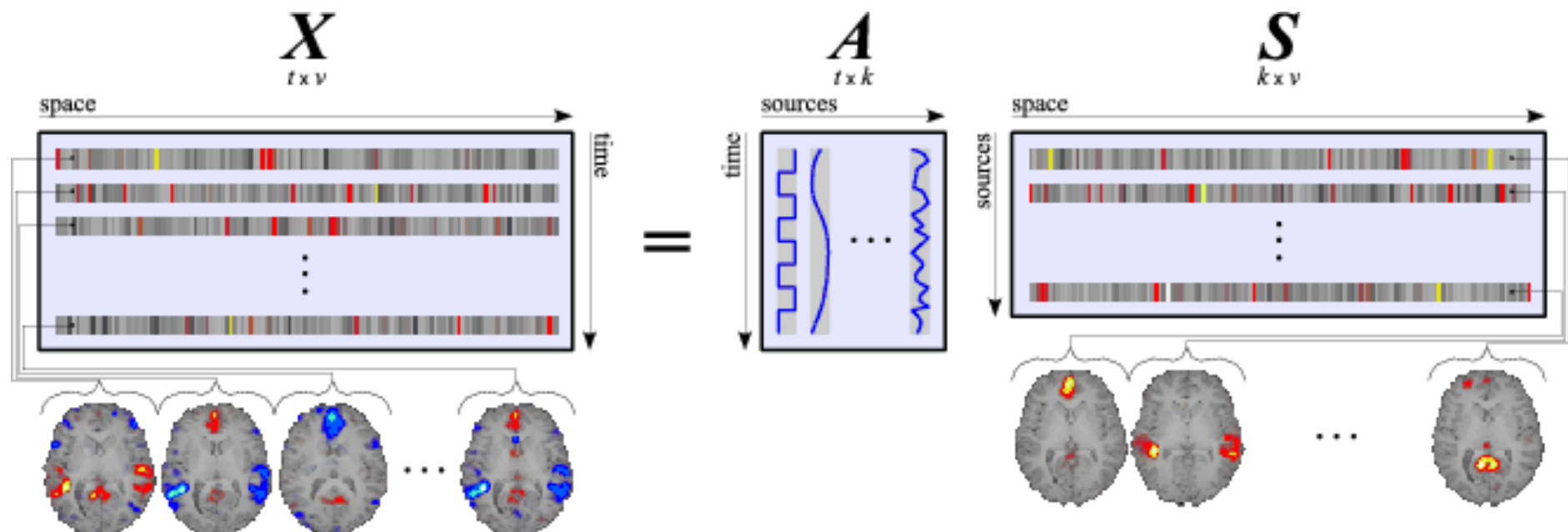


Biswal et al., *Magn Reson Med* 1995



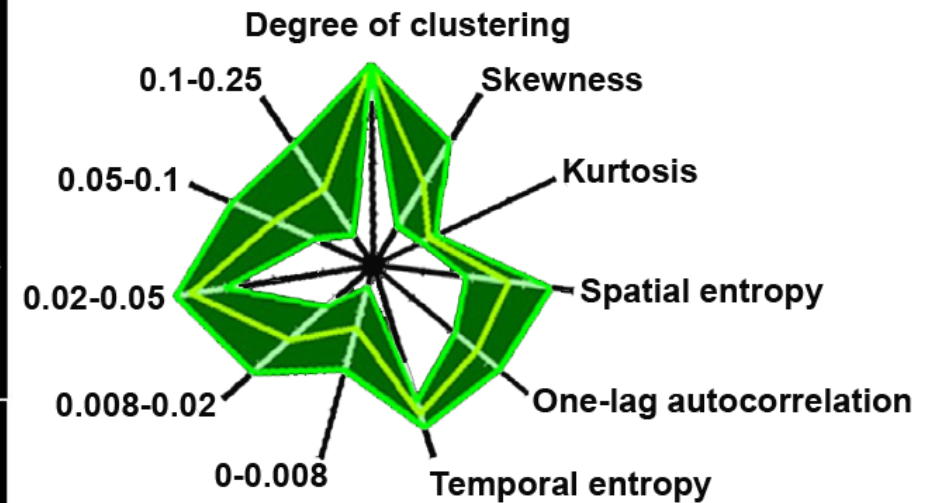
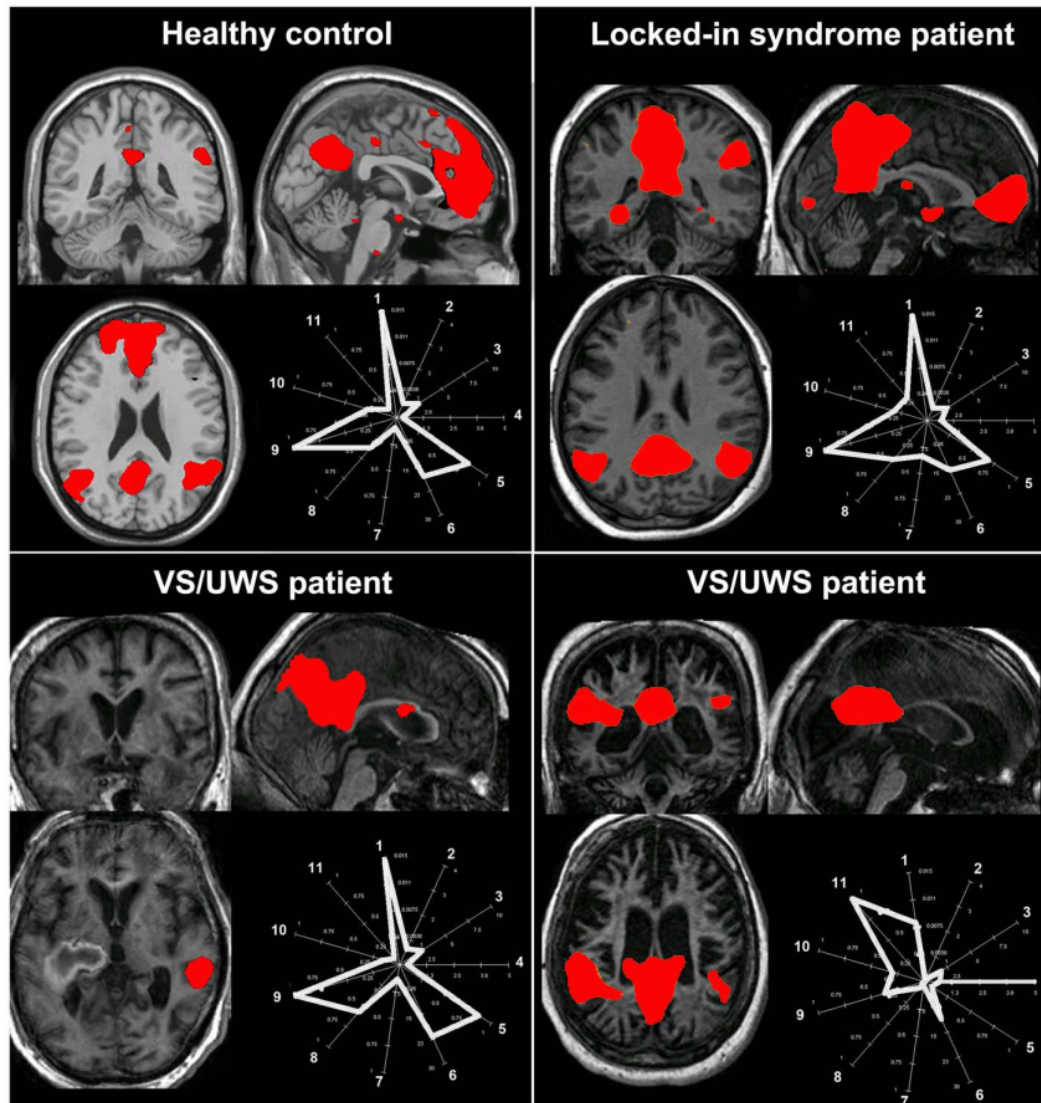
Smith et al, *PNAS* 2009

Independent component analysis (ICA)



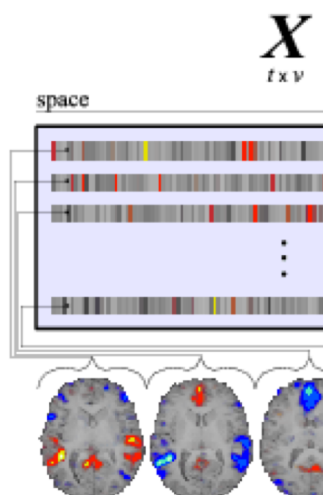
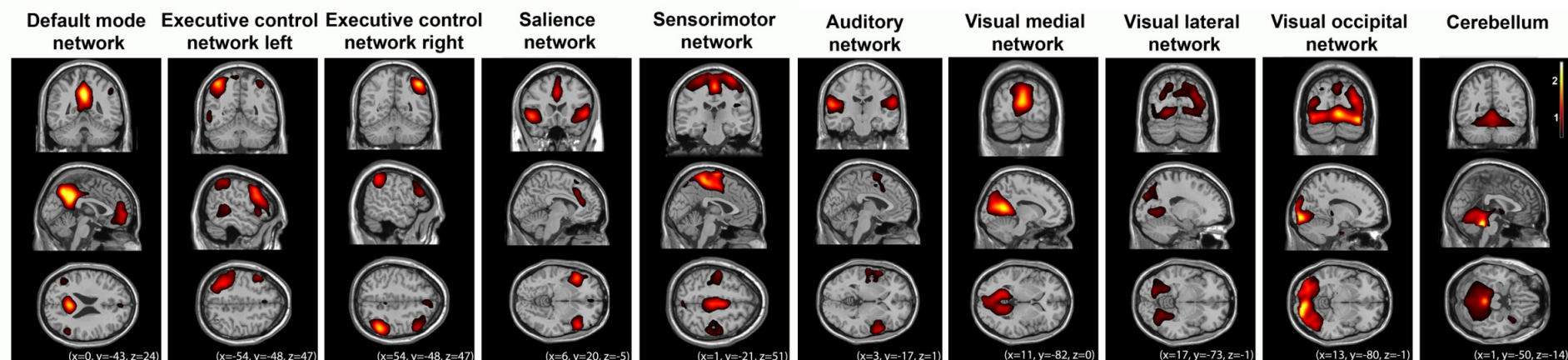


A challenge...

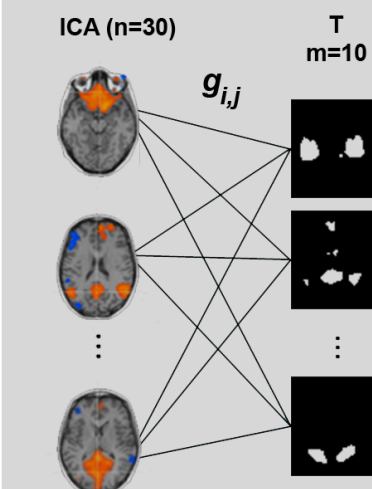




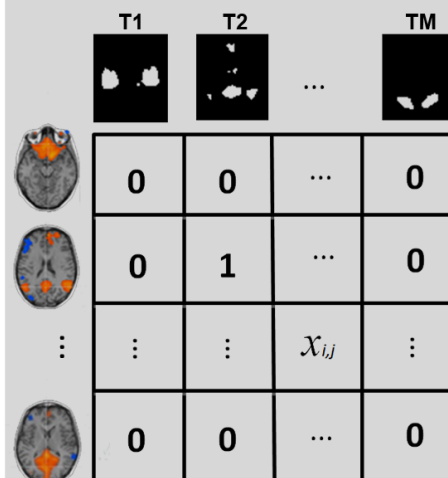
Systems-level intrinsic connectivity



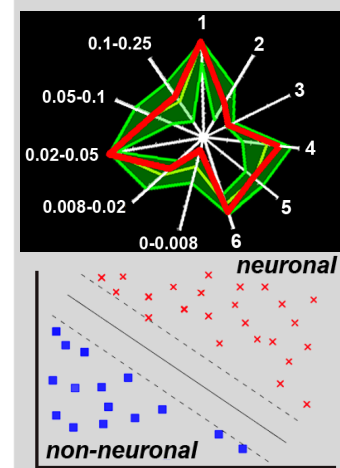
1. Goodness-of-fit calculation



2. Multiple template assignment

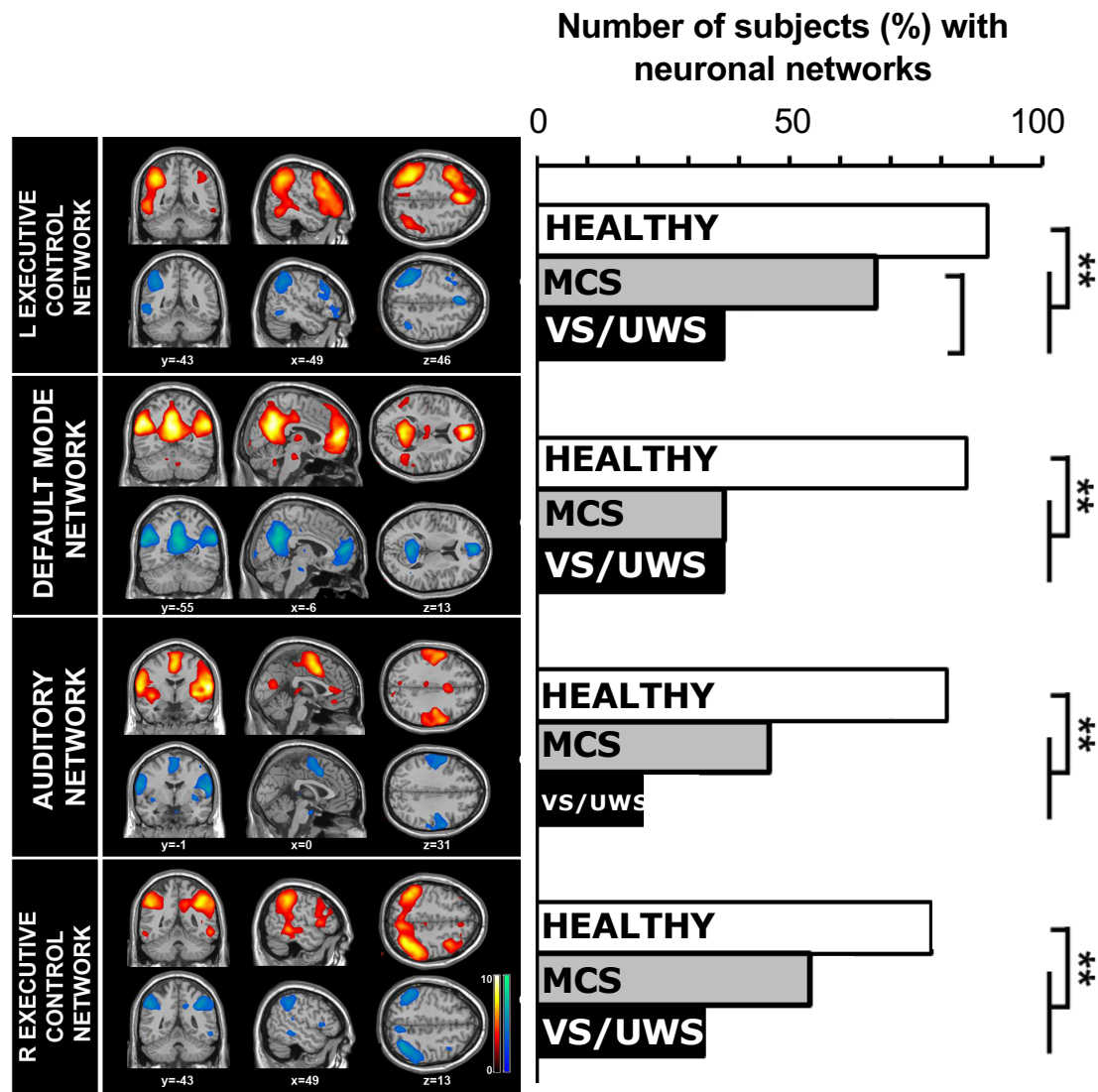


3. "Neurality" test





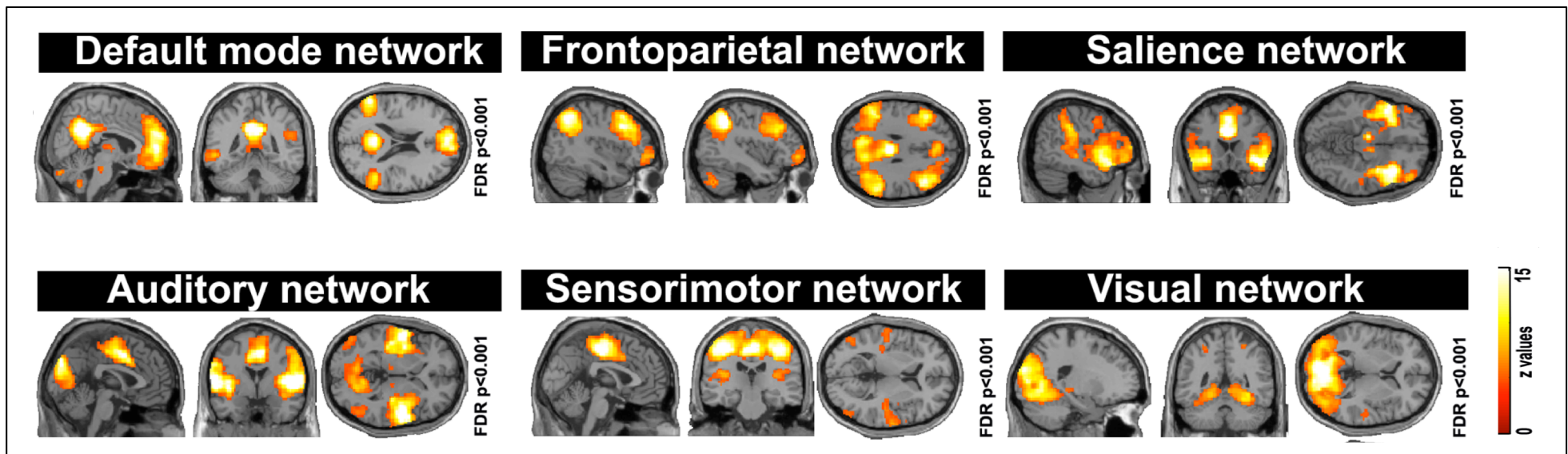
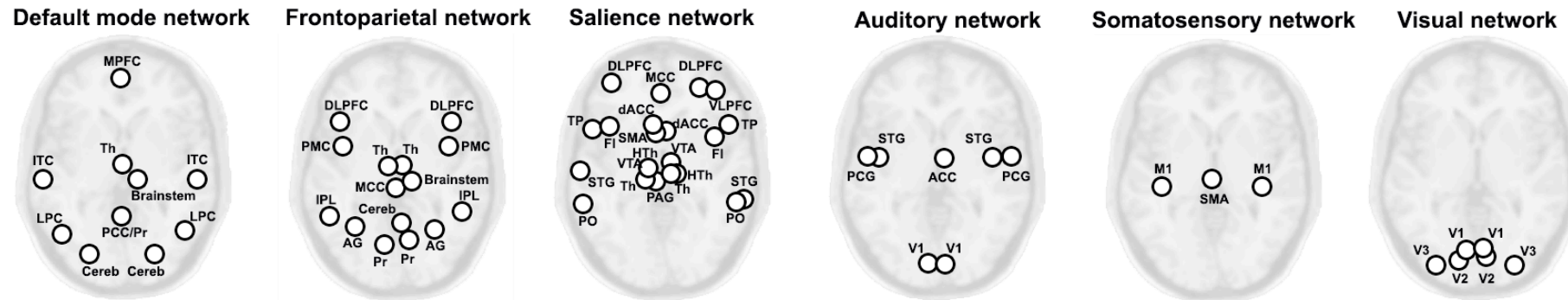
Fewer “neuronal” networks in DOC



Single-patient classification

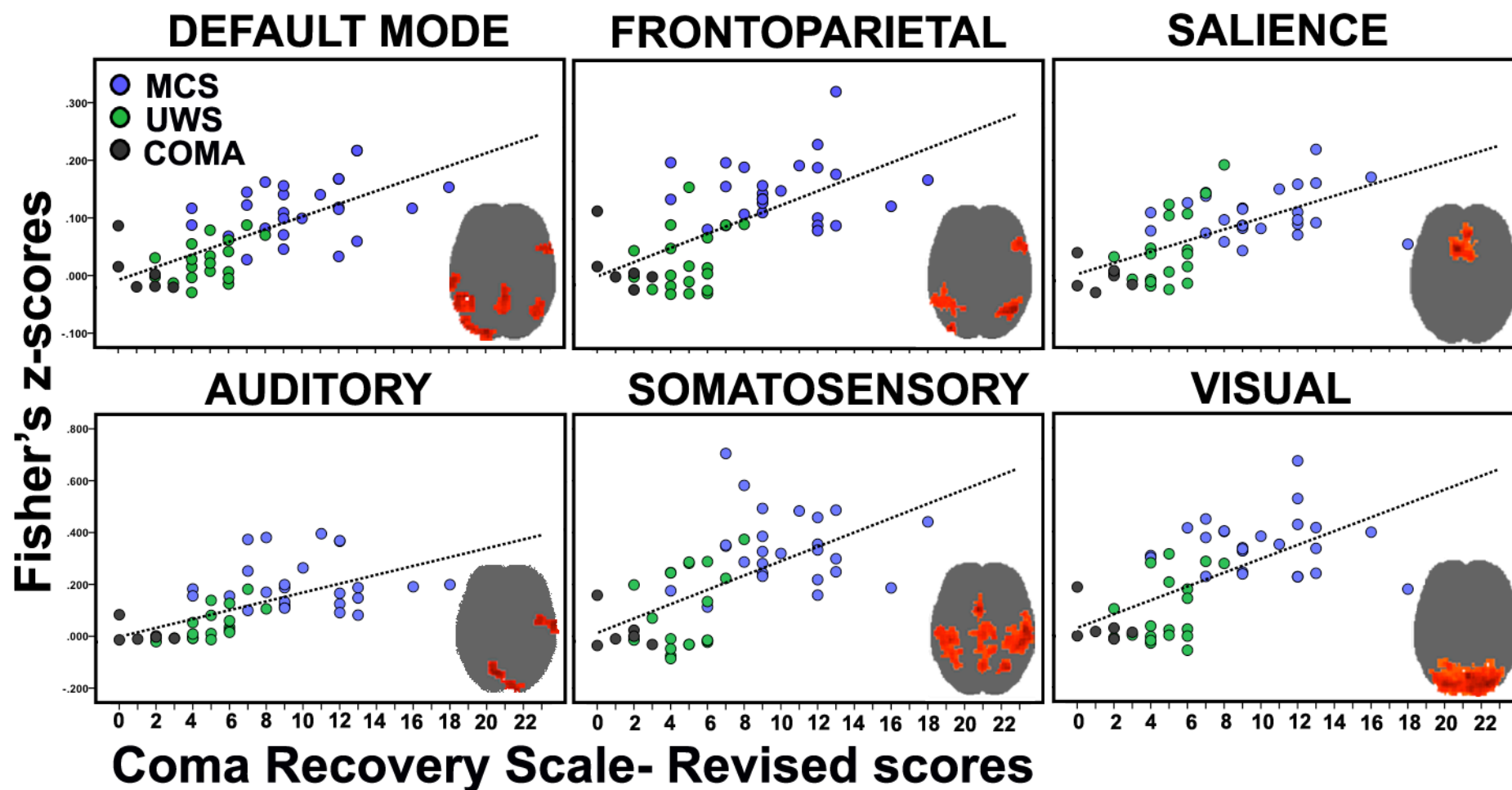
| Performance measures | Accuracy | TPR healthy | TPR patients | Selected RSNs |
|----------------------|--------------------------|-------------|--------------|---------------|
| | Healthy vs. all patients | | | |
| Neuronal | 85.3 | .82 | .87 | Auditory, DMN |

Seed-based functional connectivity





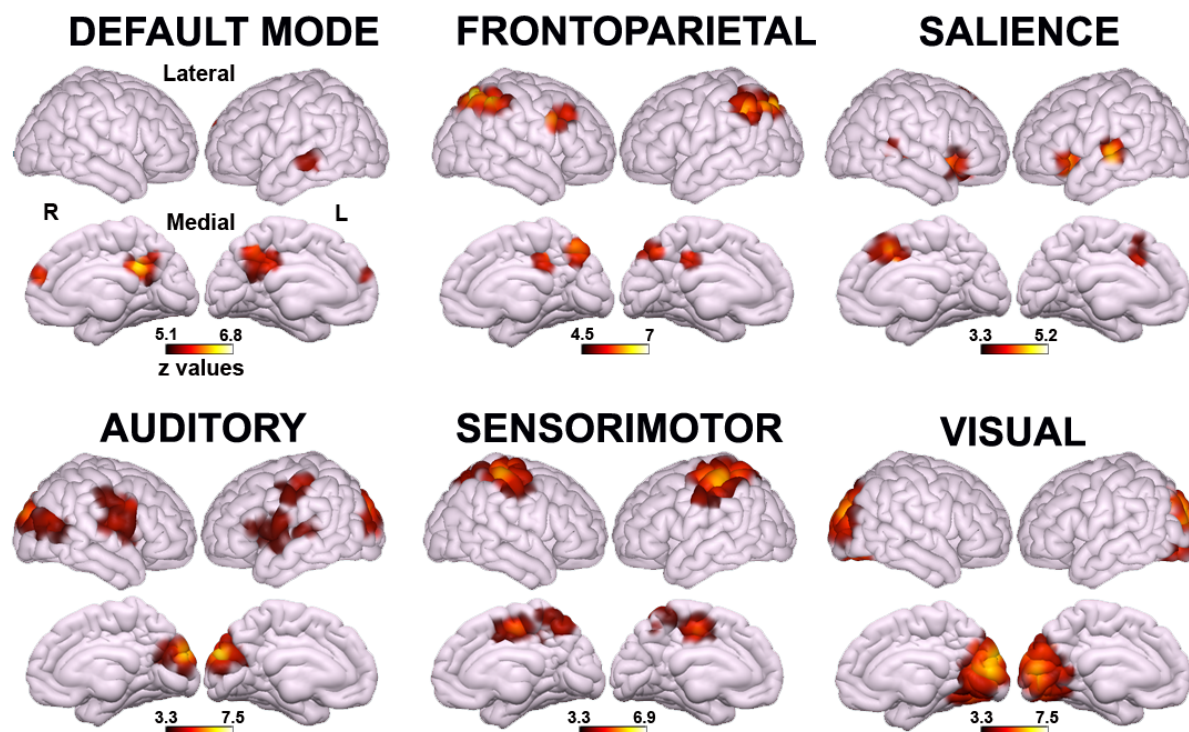
Connectivity reflects C state





Which network discriminates best?

MCS > VS/UWS

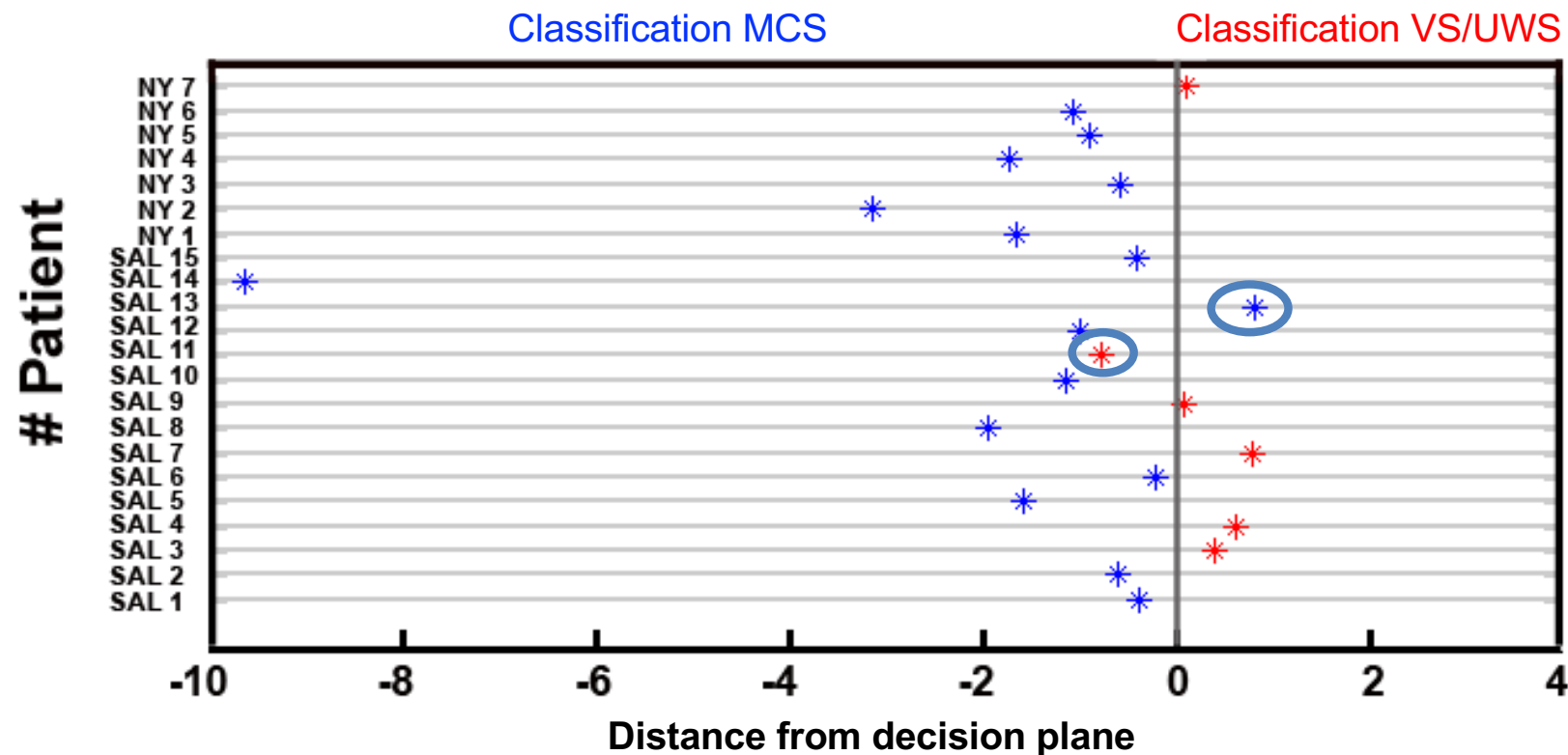
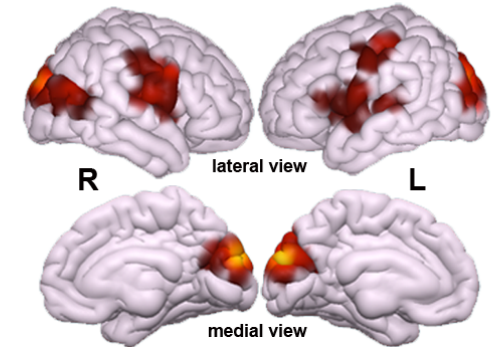


FWE $p < 0.05$ (cluster-level)

| Network | Feature selection criterion (t-test) | | | Single-feature classification | | |
|----------------|--------------------------------------|------|---------|-------------------------------|-----------|----------|
| | t value | Rank | p value | TP MCS | TN VS/UWS | Accuracy |
| Auditory | 8.32 | 1 | <.001 | 25 | 18 | 43/45 |
| Visual | 7.79 | 2 | <.001 | 23 | 15 | 38/45 |
| Default mode | 6.95 | 3 | <.001 | 23 | 15 | 38/45 |
| Frontoparietal | 6.82 | 4 | <.001 | 23 | 15 | 38/45 |
| Salience | 6.21 | 5 | <.001 | 24 | 15 | 39/45 |
| Sensorimotor | 5.87 | 6 | <.001 | 24 | 13 | 37/45 |

Crossmodal connectivity classifies DOC

- Training set: 45 DOC (26 MCS, 19 VS/UWS)
 - 14 trauma, 28 non-trauma, 3 mixed
 - 34 patients assessed >1m post-insult
- Test set: **16 MCS**, **6 VS/UWS** (M_{age} : 43y, 15 non-trauma; all chronic), from 2 different centers





Interim conclusions

RS functional connectivity :

- is linked to behavior and task performance *(Laird et al., 2011)*
- reflects physiological & pathological unconsciousness *(Heine et al, 2012)*
- permits single-patient automatic diagnosis *(Demertzi & Antonopoulos et al, 2015)*

But

it remains unclear to what extent it provides a
representative estimate of cognition

(Peterson et al, NeuroImage Clin. 2015)

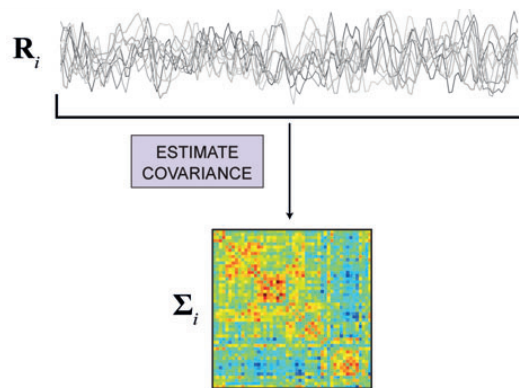


Ongoing interactions among distinct brain regions

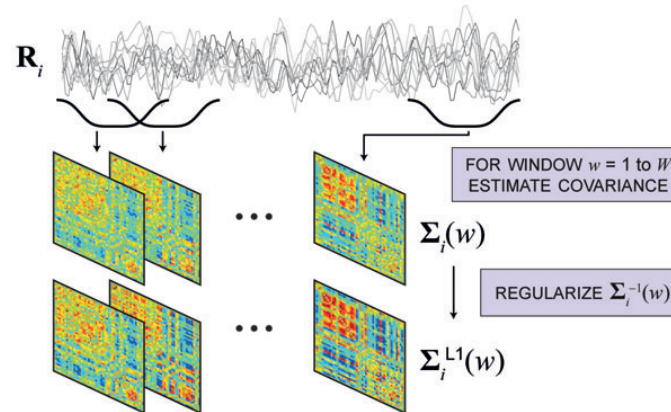
(Hutchison et al, NeuroImage 2013)

From stationarity to dynamics

Stationary fc



Time-varying fc



Dynamic

$$x_t = A \cdot x_{t-1} + \epsilon_t$$

Brain dynamics and cognition

Typical wakefulness: significance for performance, emotion and cognition

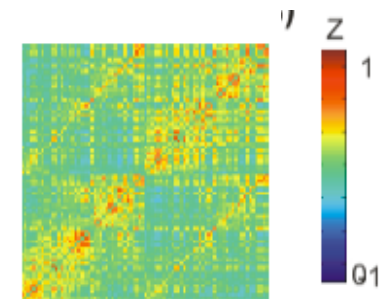
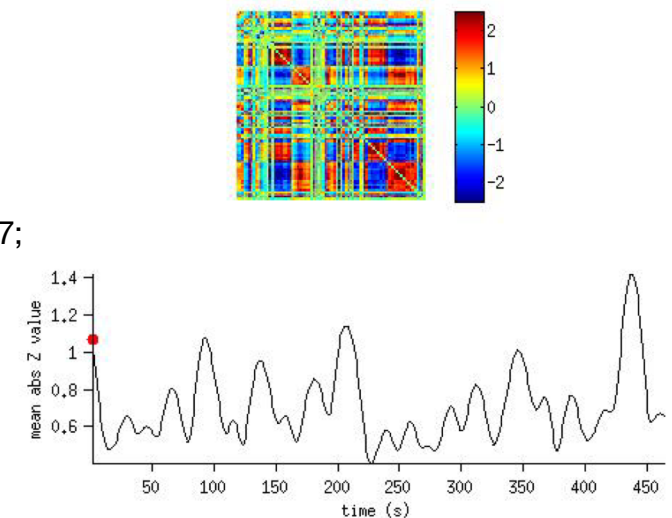
(Alavash, et al, *Neuroimage*, 2016; Shine et al., *Neuron*, 2016; Friston, *Neuroimage*, 1997; Thompson et al., *Hum. Brain Mapp*, 2013)

Unconsciousness: rigid spatiotemporal organization, less metastable dynamics

- **sleep** (Tagliazucchi et al., *PNAS* 2013; Wang, et al, *PNAS* (2016; Wilson et al., *Neuroimage* 2015; Chow et al., *PNAS* 2013)
- **anesthesia**
 - **in humans** (Tagliazucchi et al, *J. R. Soc. Interface.* 2016; Kafashan, et al, *Front. Neural Circuits*, 2016; Amico et al., *PLoS One* 2014)
 - **in animals** (Barttfeld *PNAS* . 2014); Grandjean et al., *Neuroimage*. 2017; Liang, et al, *Neuroimage* 2015).



The brain cannot map the complexity of the internal and external world
(Dehaene, et al *Trends Cogn. Sci.* 2006; Tononi et al, *Nat. Rev. Neurosci.* 2016)



Barttfeld*, Ulhig*, Sitt*, et al, *PNAS* 2015



Study cohort (N=159)

James S. McDonnell Foundation



ScienceAdvances
AAAS

Grant Type: Collaborative Activity Award, Phase I & II (2008-2017)

Main dataset

awake

| | VS/UWS | MCS | CTR |
|-------|--------|-----|-----|
| LIEGE | 17 | 23 | 21 |
| PARIS | 13 | 9 | 15 |
| NY | 6 | 10 | 11 |
| Total | 36 | 42 | 47 |

n = 125

Validation datasets

sedated

| LIEGE | |
|-------|----|
| EMCS | 3 |
| MCS | 14 |
| UWS | 6 |

n = 23

CMD

| ONTARIO | |
|---------|---|
| VS/UWS- | 6 |
| VS/UWS+ | 5 |

n = 11



Demertzi & Tagliazucchi, Dehaene, Deco, Barttfeld, Raimondo, Martial, Fernández-Espejo, Rohaut, Voss, Schiff, Owen, Laureys, Naccache, Sitt.
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Methods

EPI acquisition



Preprocessing

Slice-time correction
Realignment
Segmentation
Normalization
Smoothing
Motion outliers (ART)
aCompCor
Regressing out realignment parameters and ART outliers
Bandpass filtering [0.008-0.09Hz]

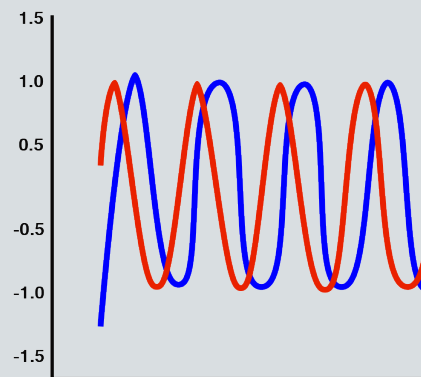
Brain parcellation

(Sphere ROIs)

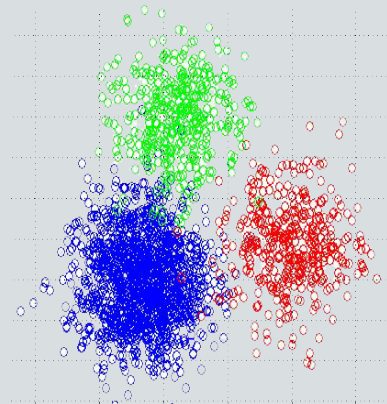


ROI timeseries extraction

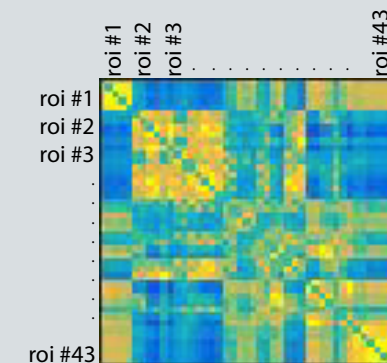
Phase analysis (Hilbert transform)



Unsupervised clustering (k-means)

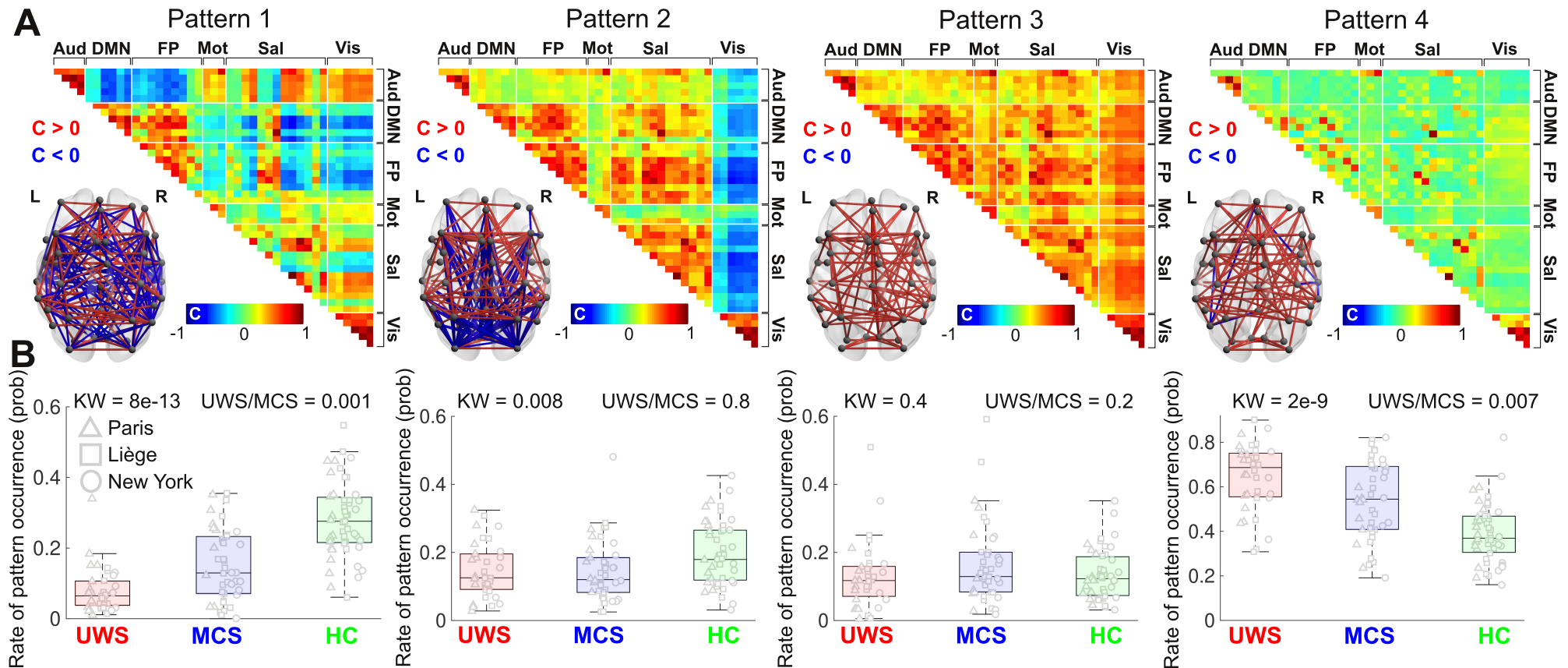


State identification (cluster centroids)



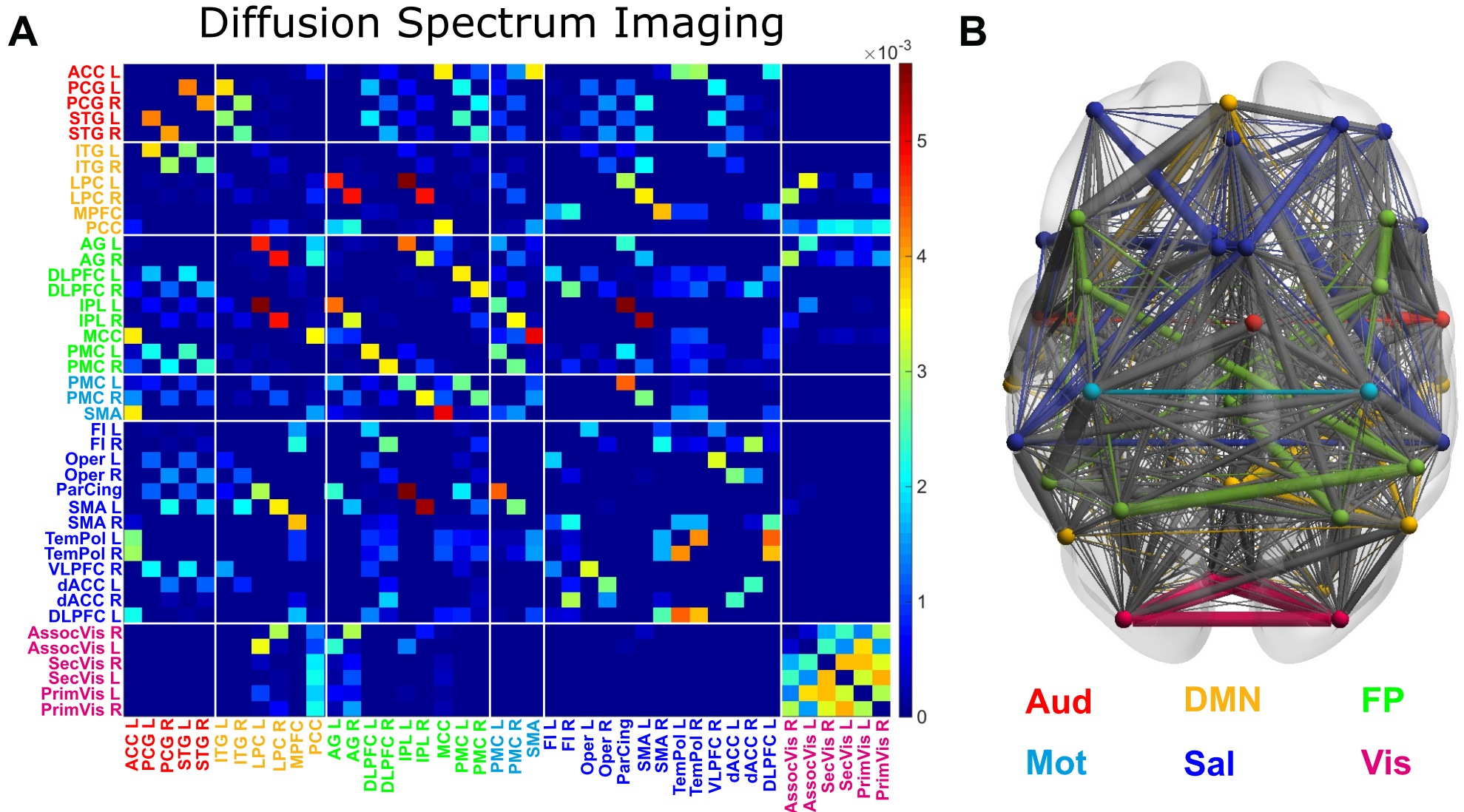


Four brain patterns





Structure-function correlation



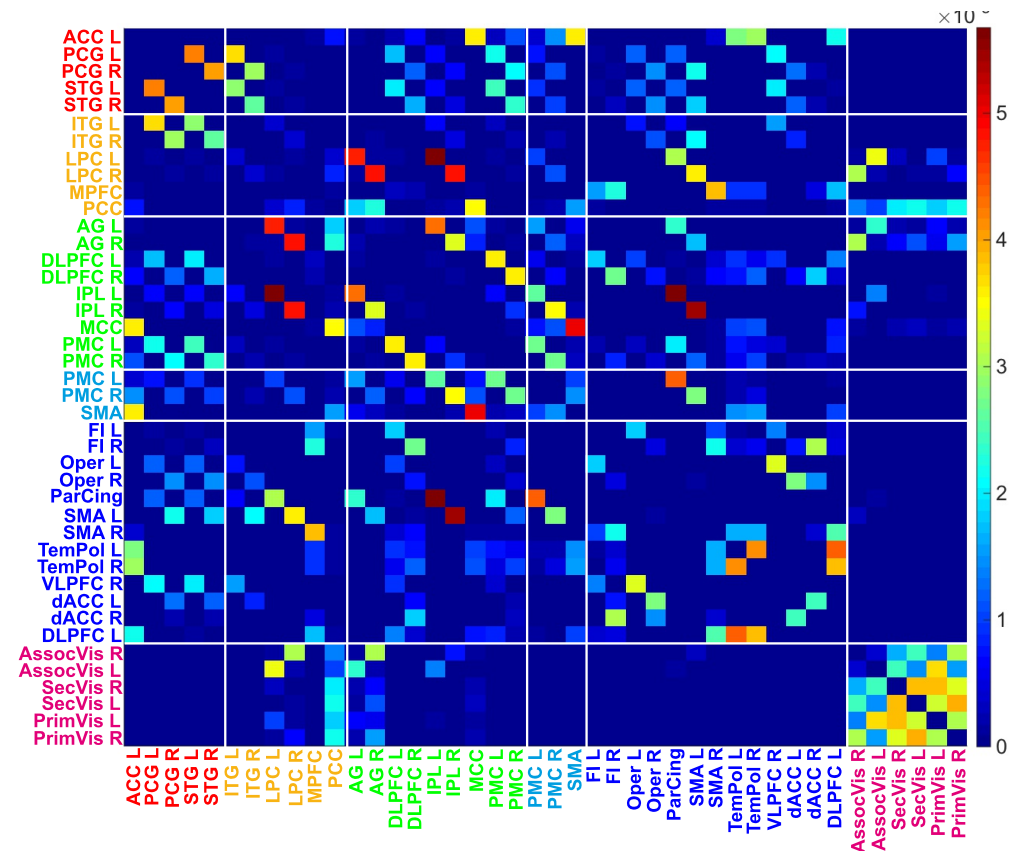
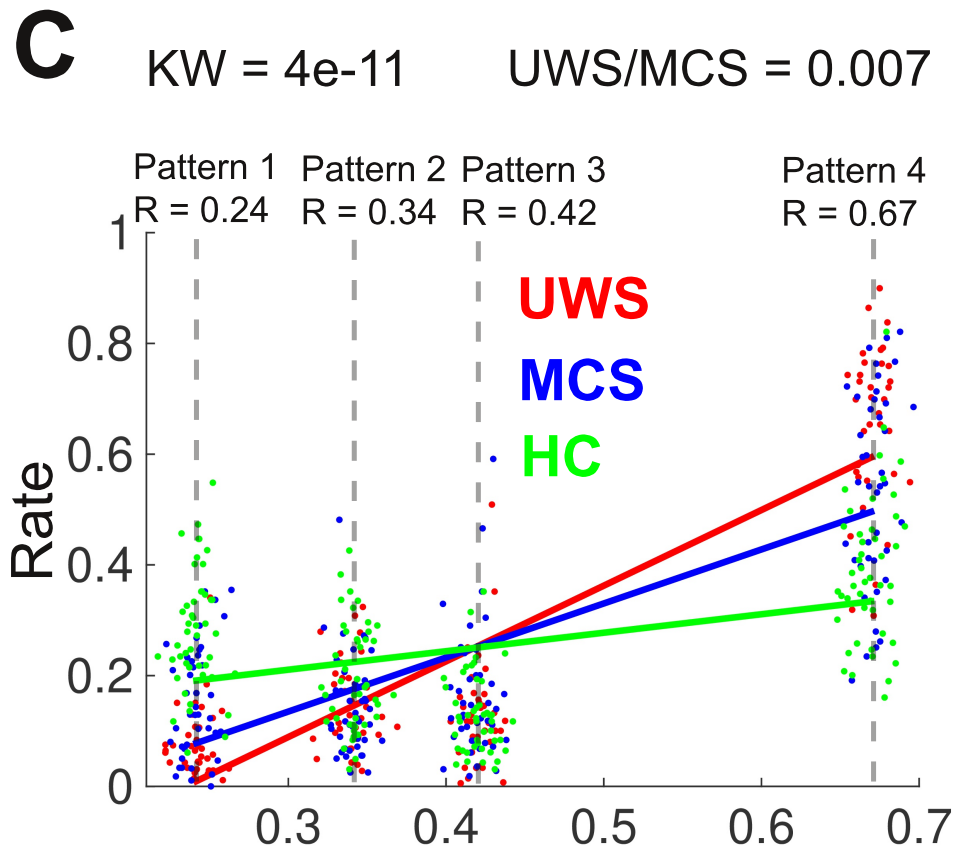
Hagmann, et al, *PLOS Biol.* 2008

Demertzi & Tagliazucchi, Dehaene, Deco, Barttfeld, Raimondo, Martial, Fernández-Espejo, Rohaut, Voss, Schiff, Owen, Laureys, Naccache, Sitt.

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Structure-function correlation





Dynamics: Markov Process

- *stochastic process that has no memory*
- *selection of next state depends only on current state, and not on prior states*
- *process is fully defined by a set of transition probabilities π_{ij}*
 π_{ij} = probability of selecting state j next, given that presently in state i .
Transition-probability matrix Π collects all π_{ij}

Transition-Probability Matrix

○ Example

- *system with three states*

$$\Pi \equiv \begin{pmatrix} \pi_{11} & \pi_{12} & \pi_{13} \\ \pi_{21} & \pi_{22} & \pi_{23} \\ \pi_{31} & \pi_{32} & \pi_{33} \end{pmatrix} = \begin{pmatrix} 0.1 & 0.5 & 0.4 \\ 0.9 & 0.1 & 0.0 \\ 0.3 & 0.3 & 0.4 \end{pmatrix}$$

If in state 1, will stay in state 1 with probability 0.1

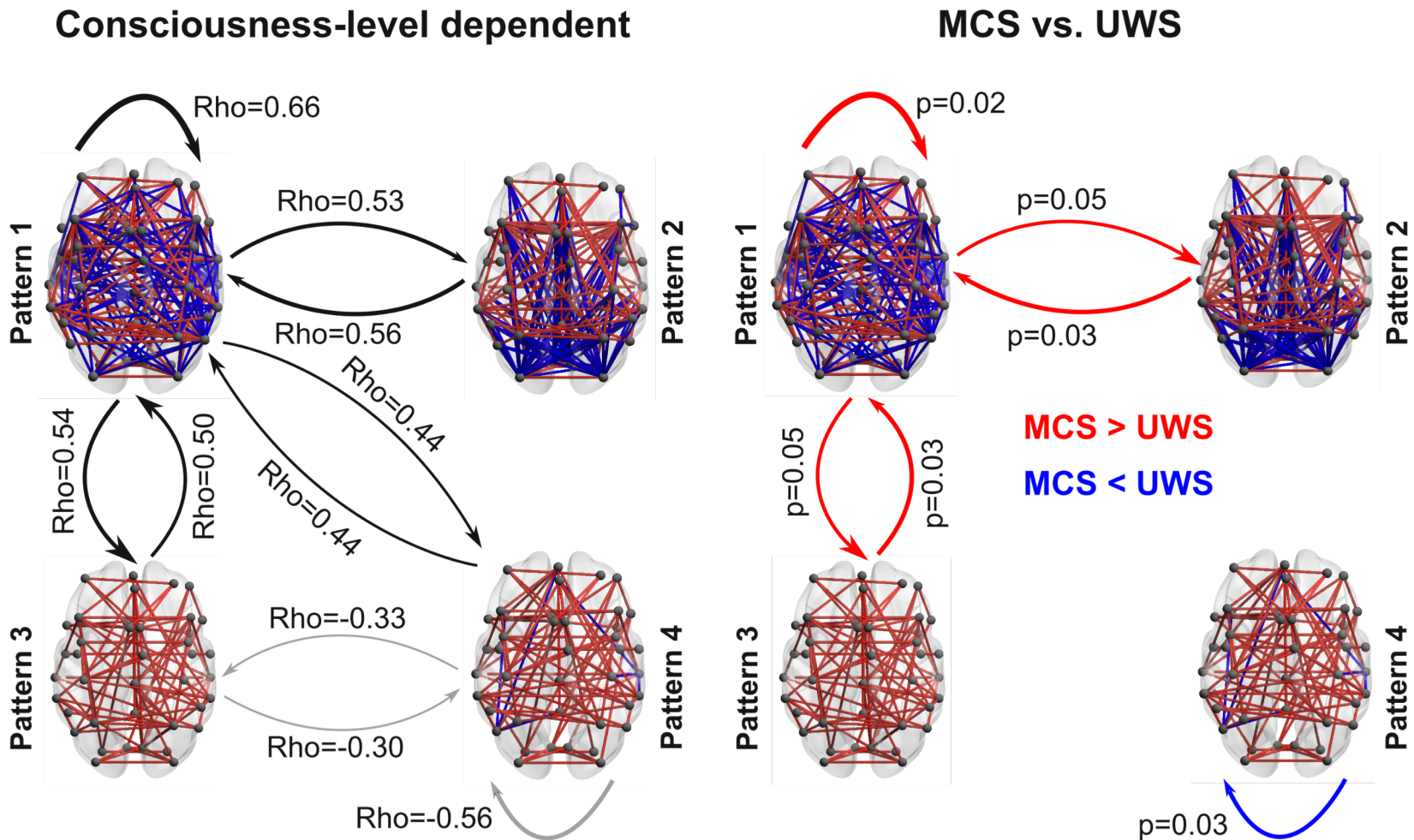
If in state 1, will move to state 3 with probability 0.4

Never go to state 3 from state 2

Dynamics

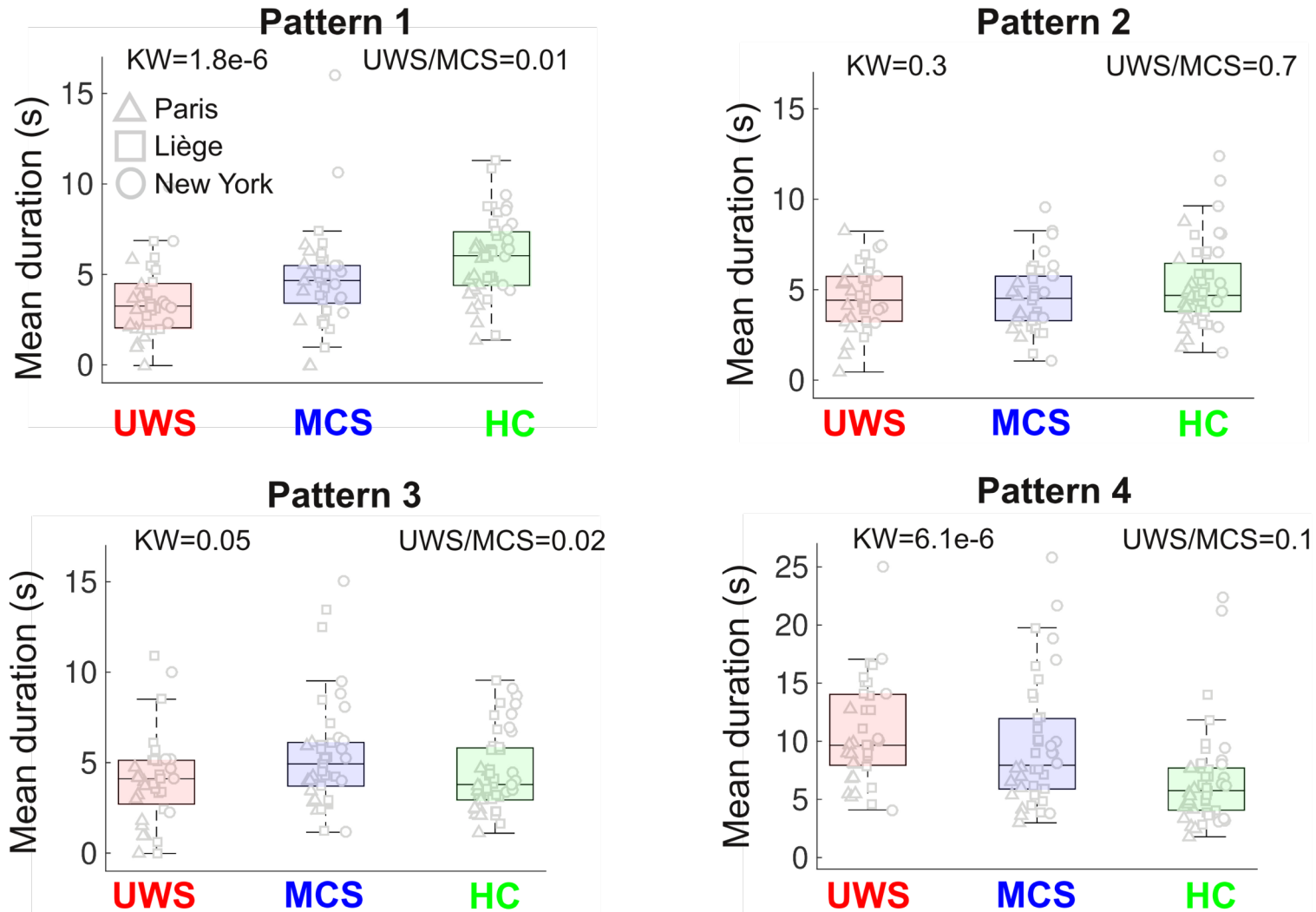
More chances to transition if in higher conscious state

A. Between-pattern transition probabilities



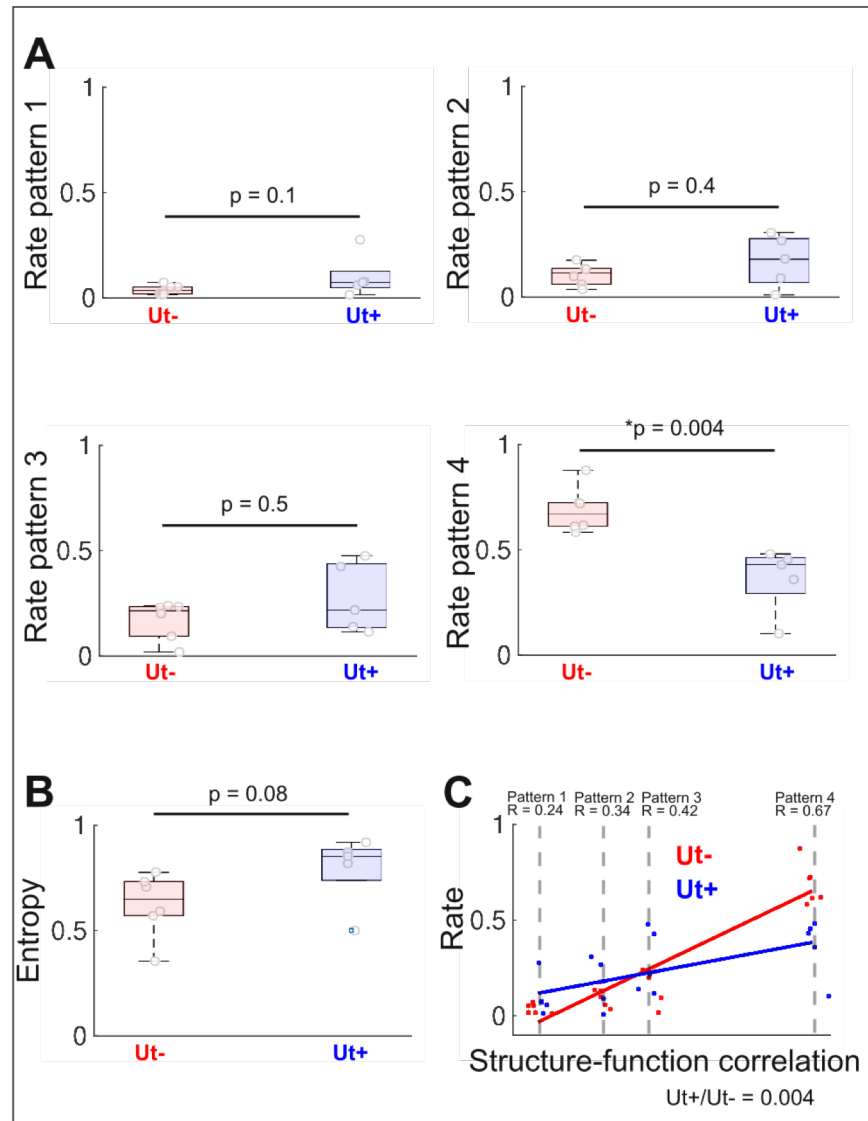
Pattern exploration is longer for more complex patterns

B. Duration of pattern occupation

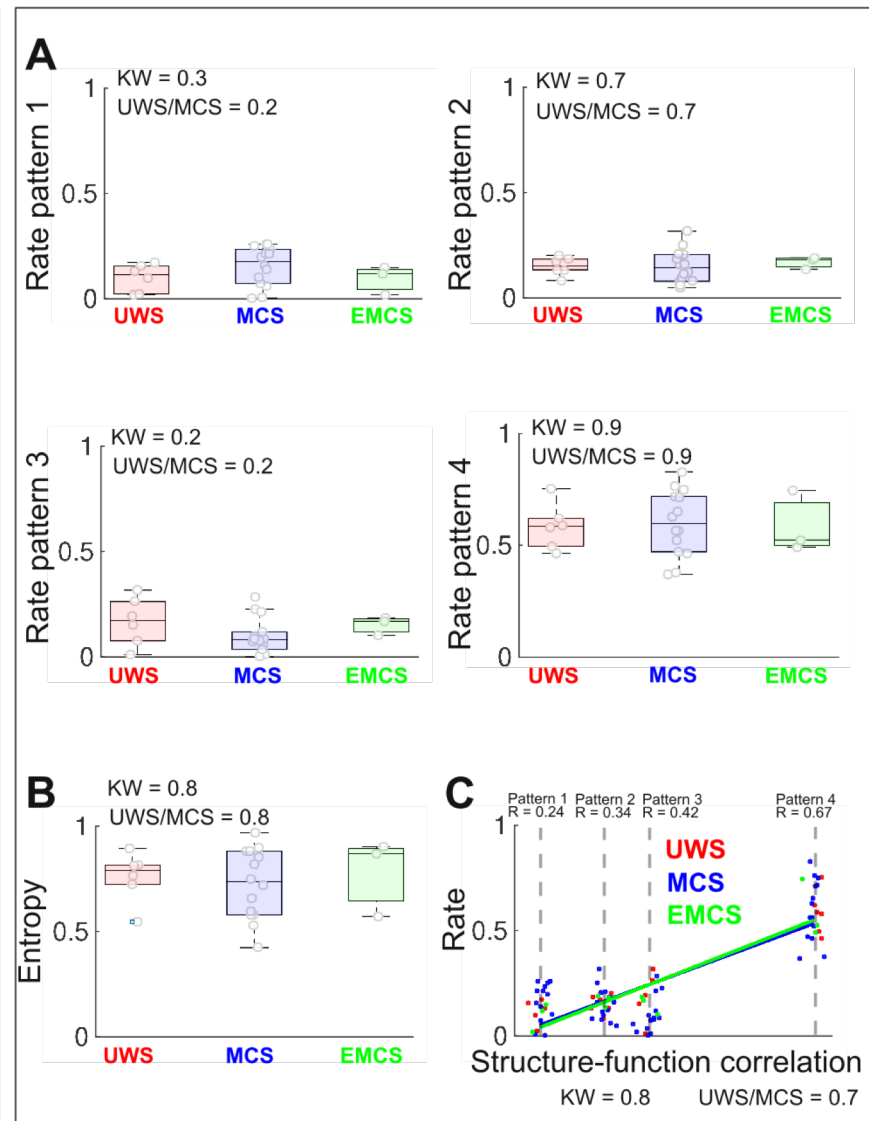


Do we measure consciousness?

Pattern prediction in cognitive-motor dissociation



Pattern prediction in anesthesia



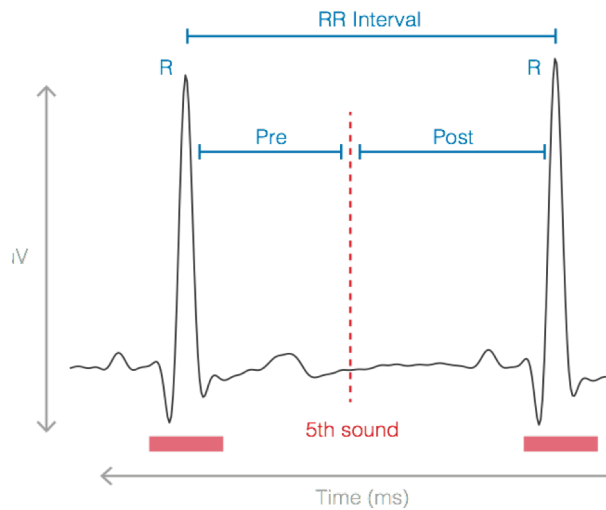


FROM BRAIN TO BRAIN-BODY INTERACTIONS

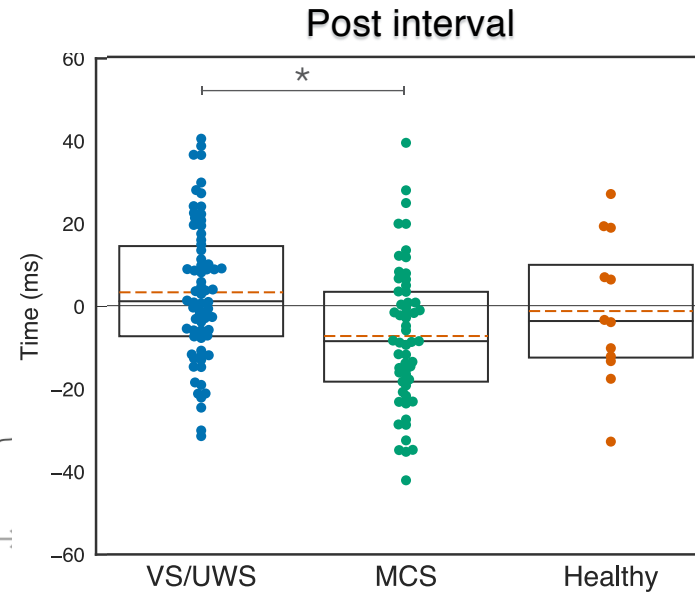
Cognitive processing modulates autonomic somatic markers



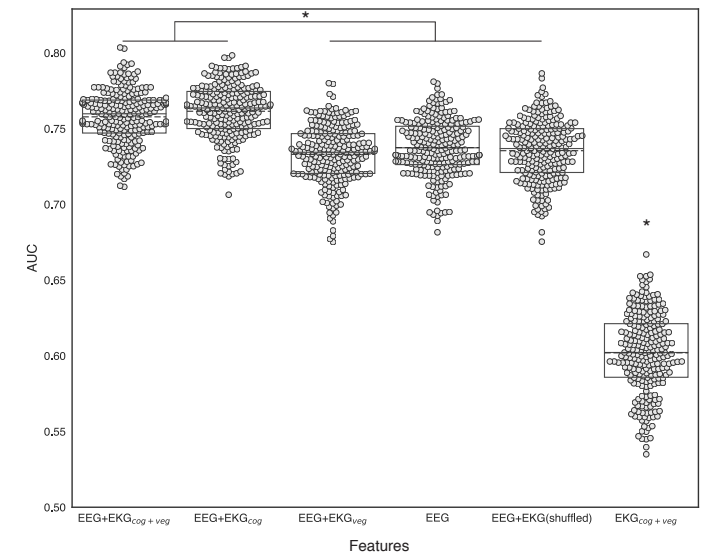
Auditory oddball paradigm



Cardiac cycle phase acceleration only in MCS

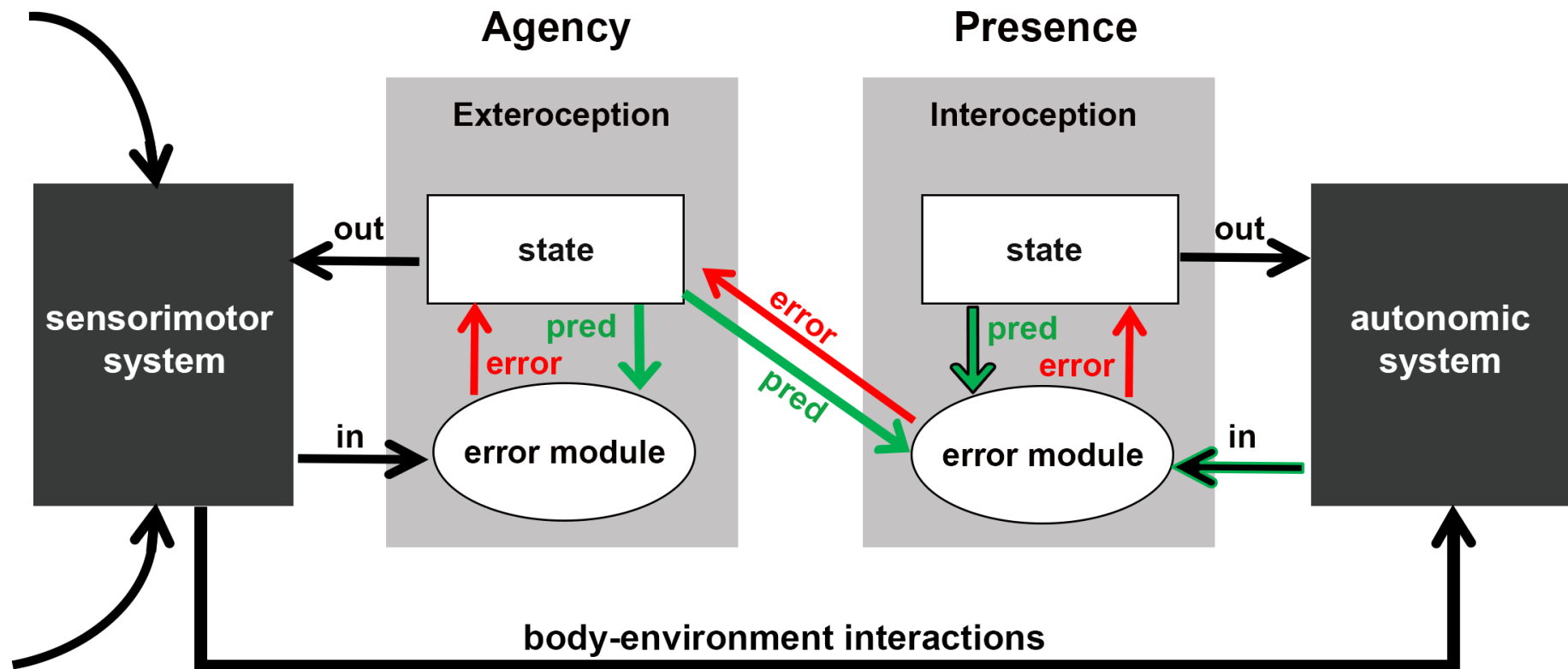


Electrocardiographic markers carry independent information from EEG





Which model for Unconsciousness?



!Apply to our lab!



Taken together...

Consciousness needs a brain which:

- is intrinsically organized
- shows complexity
- shows dynamic flexibility

Consciousness as brain-body interactions

Consciousness as active inference



Thank you

Coma Science Group & PICNIC Lab

The departments of Neurology and Radiology in Liège & Paris

**...and mostly
patients and their families!**

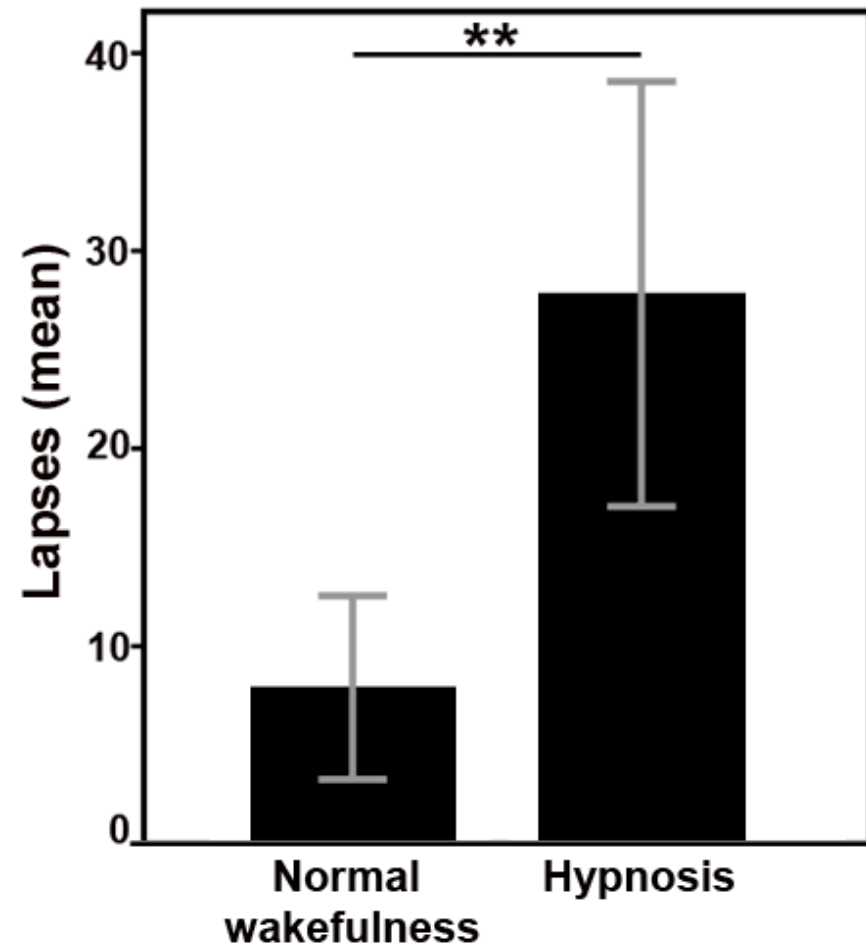
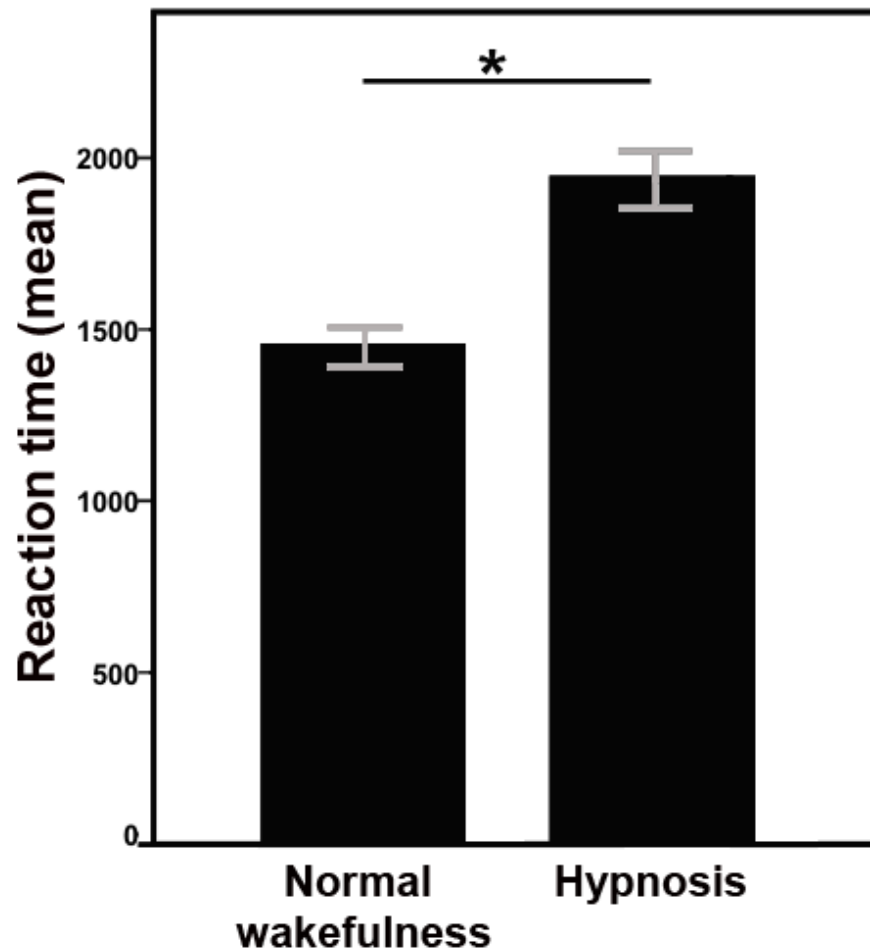


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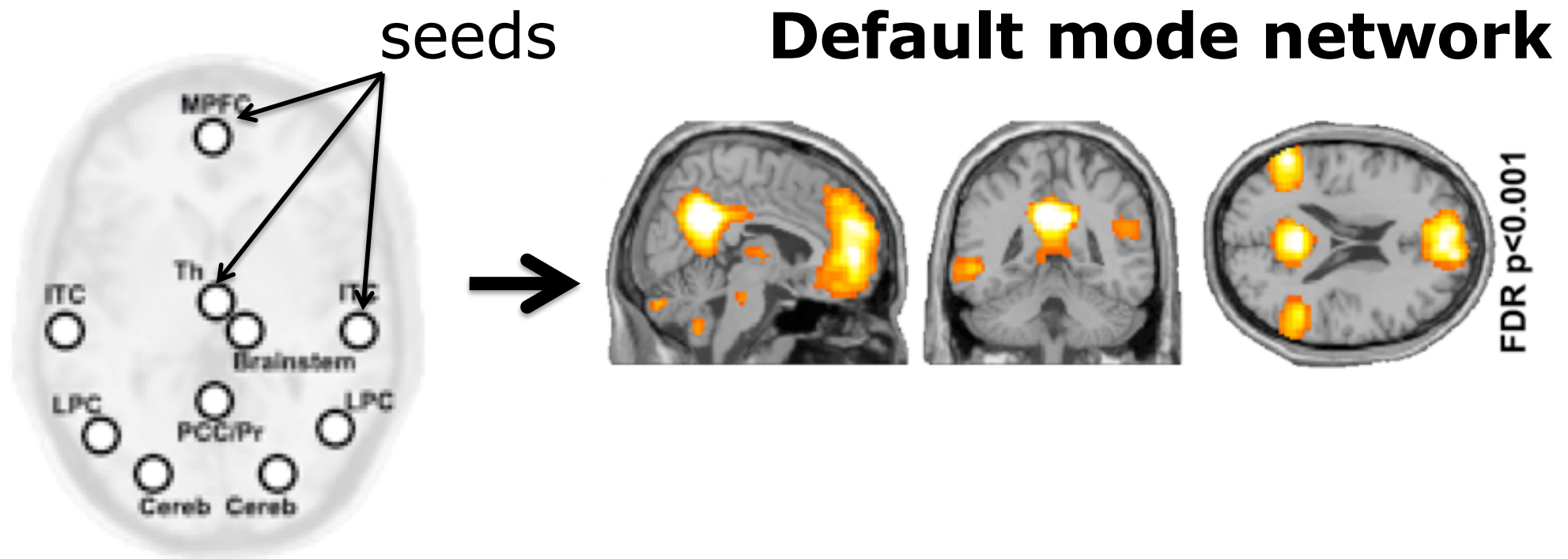
 ADemertzi



Anticorrelated connectivity is modified in hypnosis-Behavior

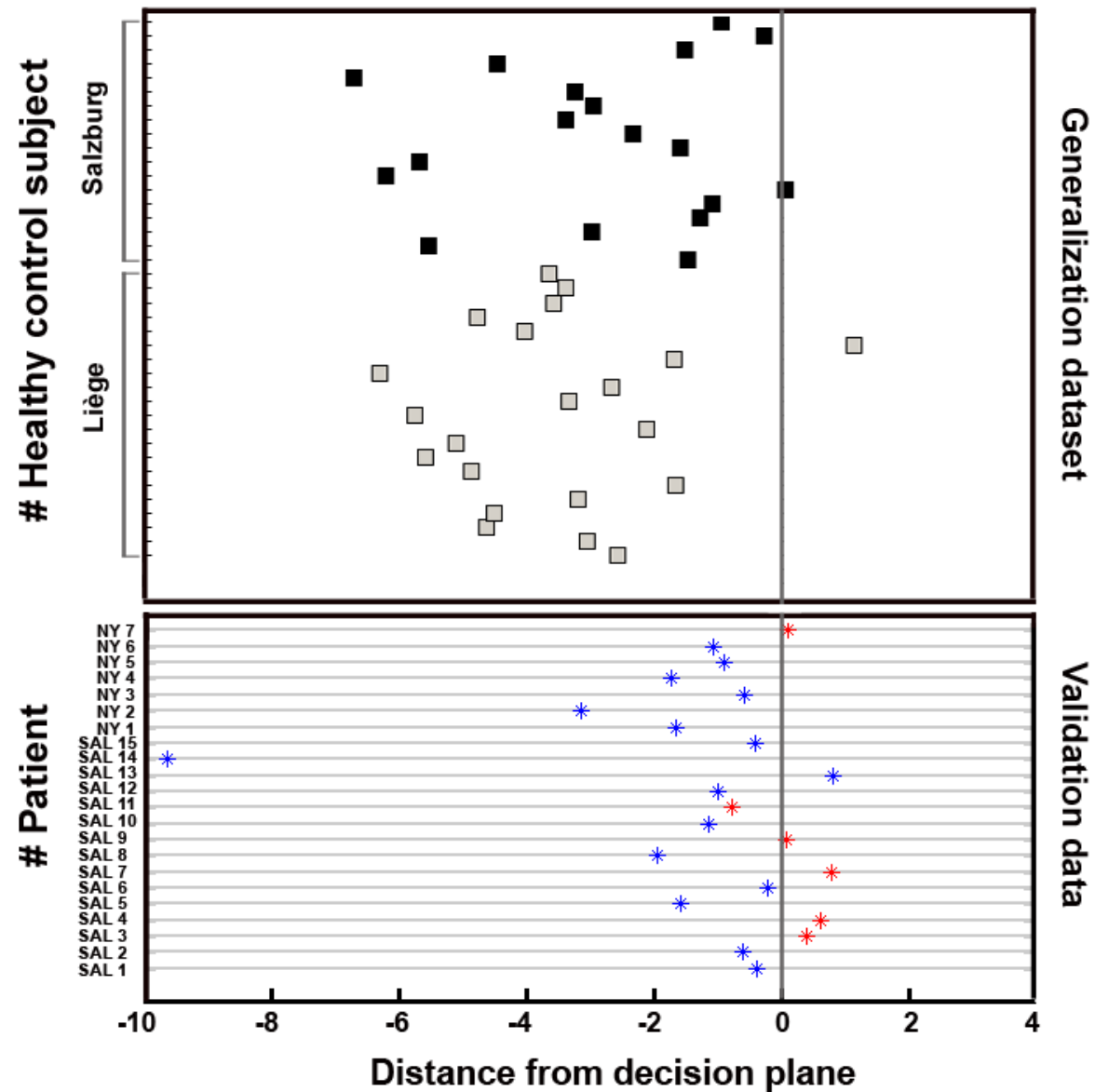


Seed-based functional connectivity

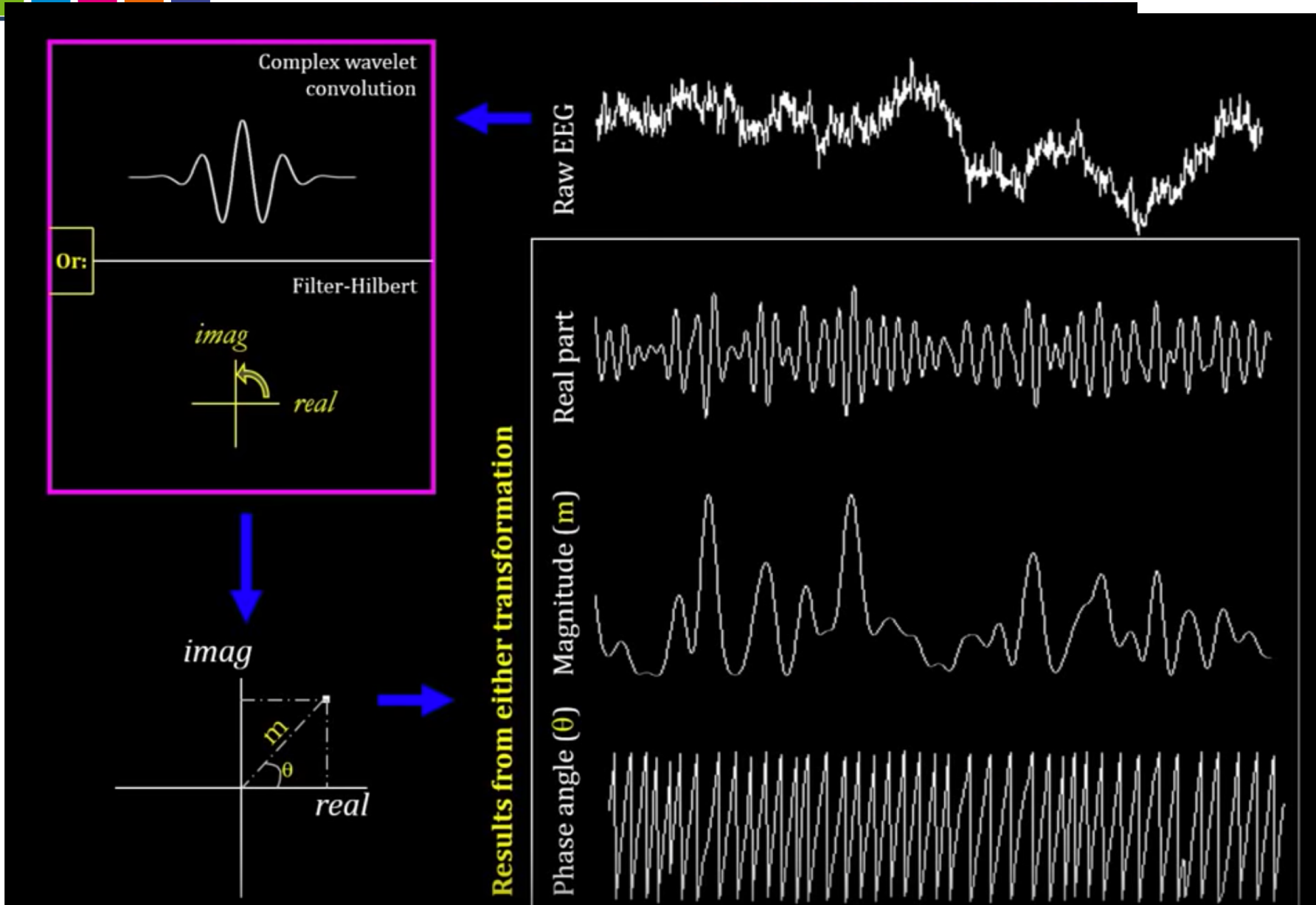




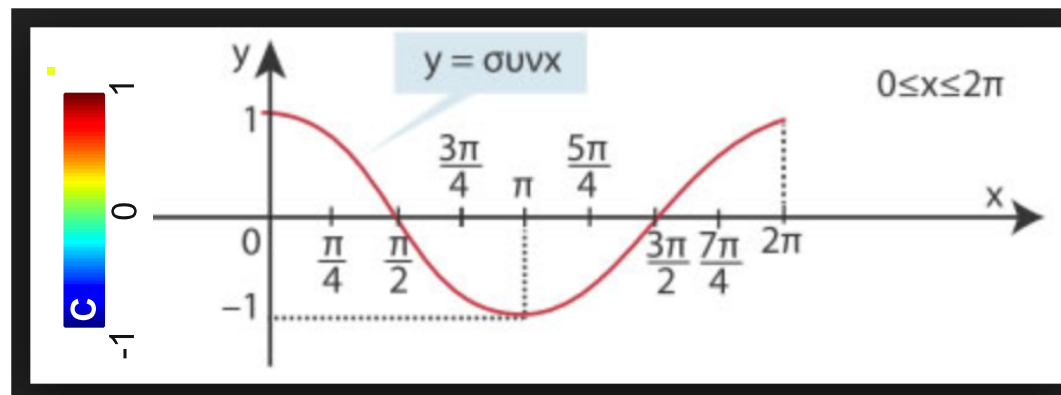
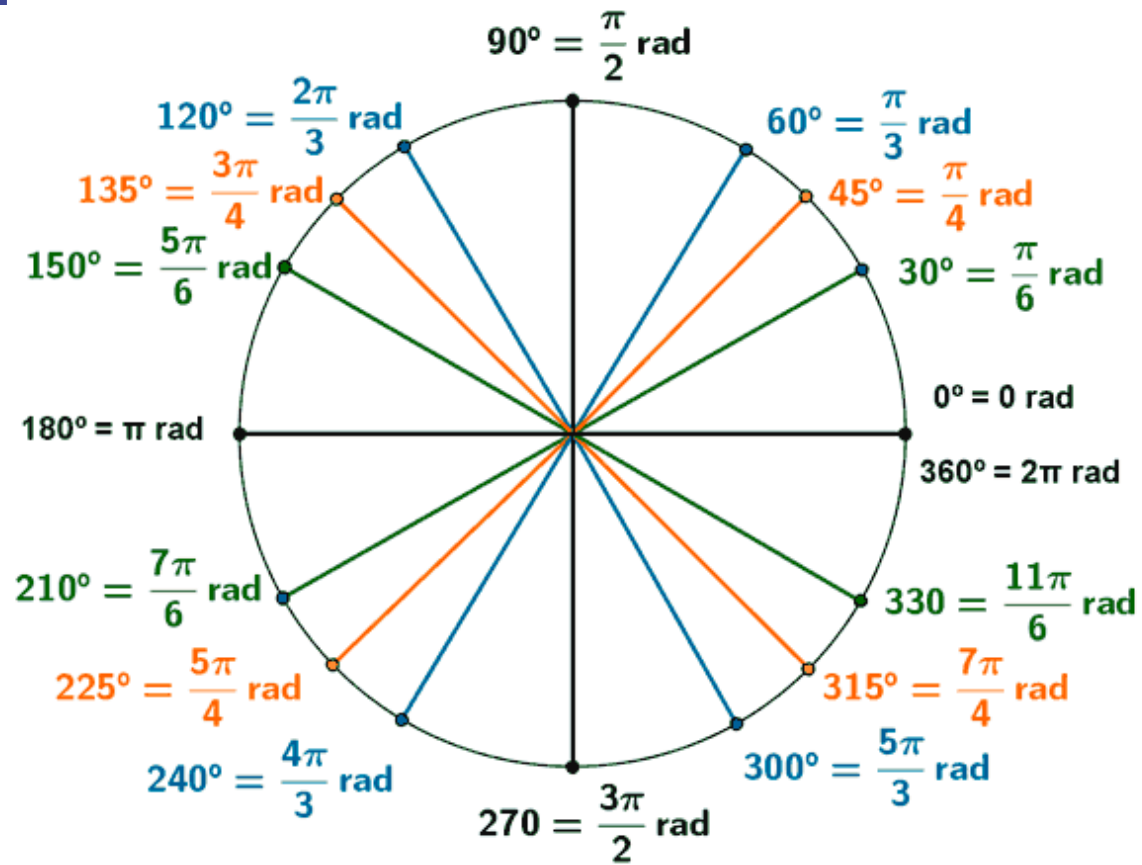
Classifier generalizes to healthy



The Hilbert transform

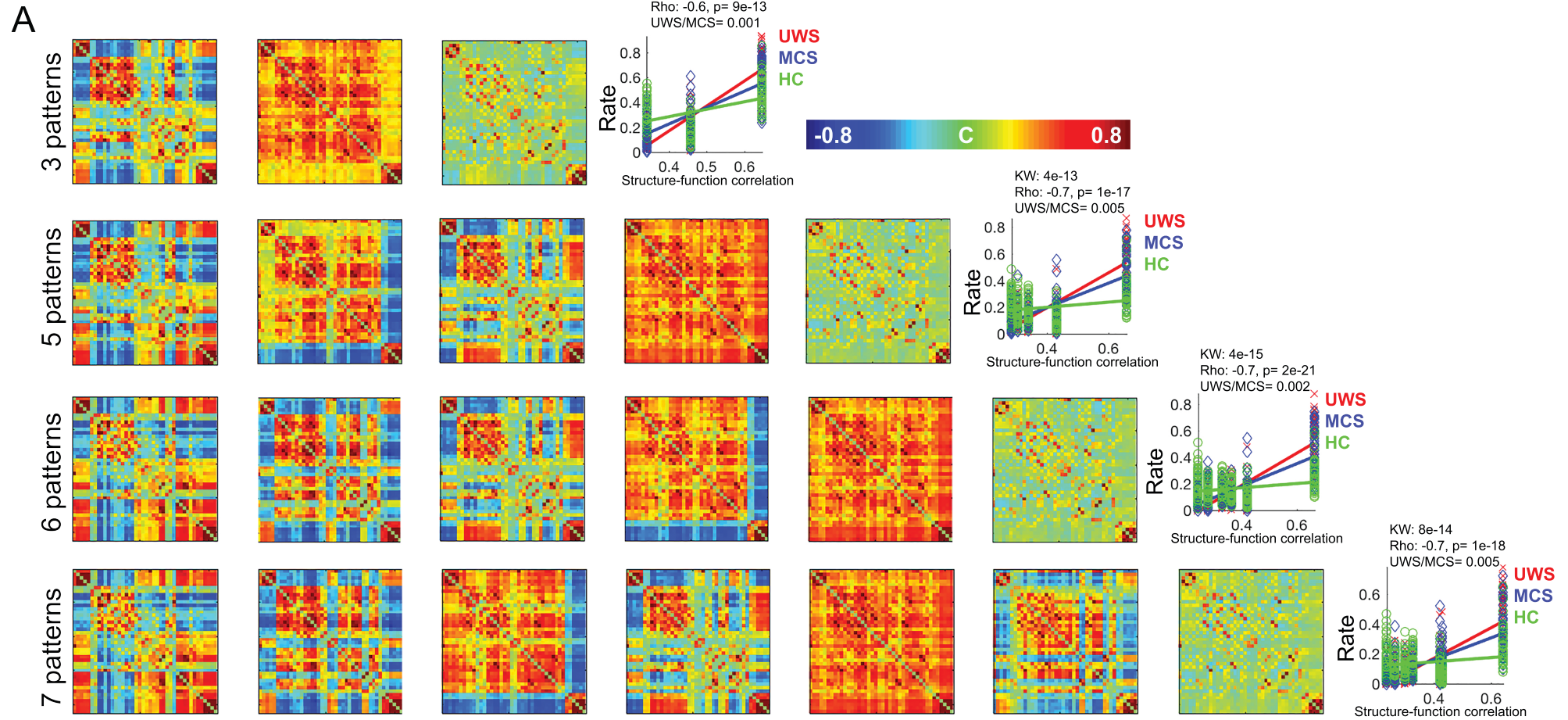


Phase coherence





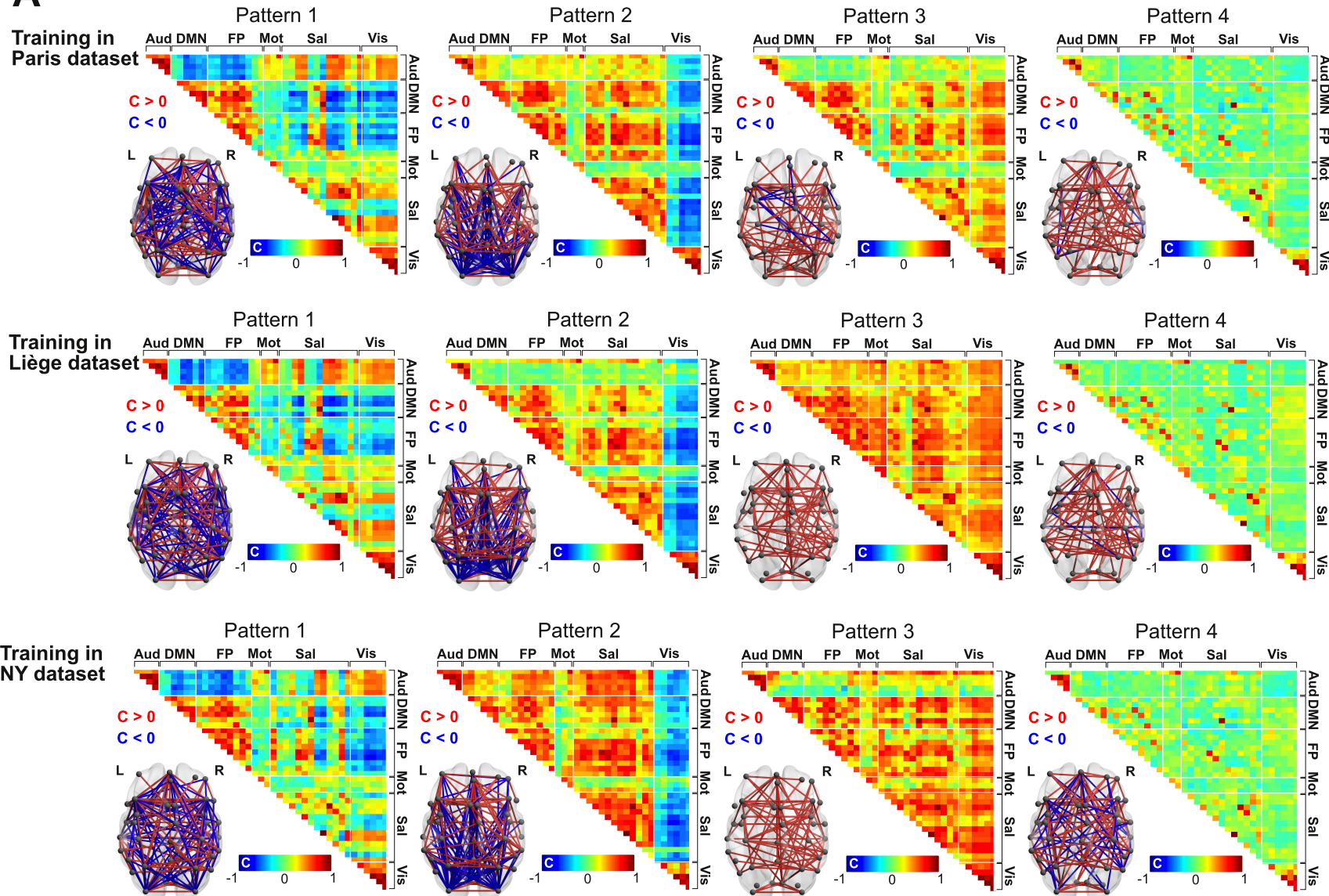
Patterns (different k)





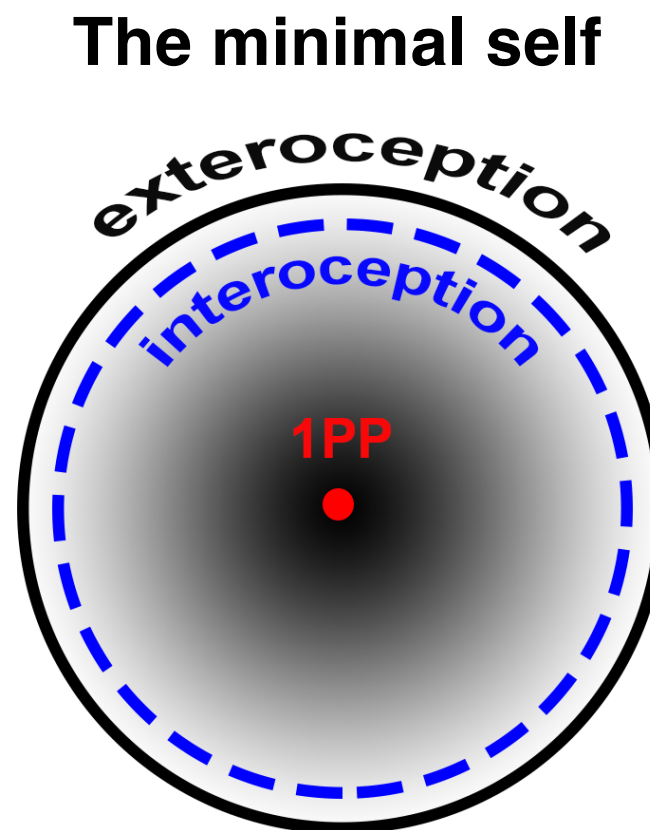
Patterns (per site)

A





Self = Consciousness?





Anticorrelated brain systems

